

American Journal of Obstetrics and Gynecology

VOL. 53

MAY, 1947

No. 5

Transactions of the Central Association of Obstetricians and Gynecologists

Fourteenth Annual Meeting

Chicago, Ill., Sept. 19 to 21, 1946

PRESIDENTIAL ADDRESS*

Individualism

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WHEN I took office as your president in 1941, I was deeply appreciative of the honor you had given me. This Association occupies a unique position in our specialty. While it is the largest Association of Obstetricians and Gynecologists in the country, and while its ever lengthening list of applicants for membership attest its popularity, mere size and popularity do not explain its importance. That importance, it seems to me, lies in qualities much deeper; qualities of mind and heart, placed there by its founders; qualities of intellect, insight, and idealism that have grown with the years and, even in the confusion and chaos of the years of war, have not been lost.

I hope that never again will it be necessary for this Association to have one president as long as it has had me! Charge that also to the destruction and desolation wrought by war! You charged me, along with the other officers and members of the Executive Committee, with the responsibility of keeping this Association alive during those trying years. We have done so. Not only have we kept it alive, but we have strengthened it so that its prestige has grown, its financial condition is sound, its ability to produce sound, sensible, and scientific contributions to obstetric and gynecologic literature has never been higher, and its good fellowship, always a noteworthy feature of our Association, remains pre-eminent. Your executive committee has been most faithful in carrying out its trusteeship by its attendance upon annual meetings even though time was limited, travel difficult and personal expense and inconvenience, considerable.

The founders of the Central Association of Obstetricians and Gynecologists were men of vision. They were individualists and, sometimes, their individual-

*Delivered at the Fourteenth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Chicago, Ill., Sept. 19 to 21, 1946.

ism was of the "rugged" variety. It is fortunate for us that this was so. They founded an association for the encouragement and promotion of the study and practice of obstetrics and gynecology, and they based their hopes for its success on the individual enthusiasm of the younger generations of obstetricians and gynecologists who would comprise its membership. At the same time, they recognized that enthusiasm needed experience to guide it. They supplied that experience in many ways during the early years of this Association's life, but, always, with the emphasis upon the individual. From the combination of enthusiasm and experience has grown an individualism which I predict can and will play a vital part in shaping our future. I make no apology for selecting "Individualism" as the title for these remarks.

It was along in 1932 that the most recent edition of "The Forgotten Man" first made his appearance. I have no quarrel with him, nor with his equally vague brother of an earlier generation, "The Common Man." His advent did not indicate any strange obstetric phenomenon, although it did bear the earmarks of a political conception. History has recorded similar conceptions. The only serious fault I have to find is the shallow thinking which seeks to put a premium on mediocrity—for a political consideration. Now we have reached the point where both the "forgotten" and the "common" man resent these designations and both find themselves challenging the very political thinking which created them, with results which merely accentuate the general confusion.

Mediocrity has a way of infiltrating all walks of life. The fear of rising above the crowd, of being different, is not a characteristic alone of the "bobby-sox" brigade, of women who follow bizarre styles in hats, of politicians or of preachers; but it has a way of infiltrating even the medical profession! The tragedy lies in the fact that, when we sink to the level of mediocrity, we lay ourselves open to that next step in mass psychology, regimentation.

Maybe, sometime during the past five years, you have heard the word, "regimentation," applied to our profession! We have been attacked by those who would add to the self-imposed discipline which we cheerfully accepted in time of war, a discipline which no American, worthy of the name, will tolerate; a discipline which would regiment our profession into the position of subservient employees of a bureaucratic state. If we completely attain this low estate, now being so thoughtfully prepared for us by a host of starry-eyed professional "doers of good to people," we will, indeed, come to know both the "forgotten" and the "common" man, for his dual and dull personality will dwell in us.

This is not a pleasing prospect, nor do I believe that it is necessary. But I believe that it is inevitable unless we think and act clearly along some rather definite lines. It seems so difficult for us to grasp the most obvious truth! Some two thousand years ago, the Master of men stated, "He that would be great among you, let him be as your servant." That was, and still is, a challenge to the individual. There can be no finer or more fitting motto for individualism as represented in our ranks than this. No group, no profession throughout the world, has a greater right to adopt that motto than has the medical profession of America.

Individualism does not come through mass production or the assembly line, and yet it has made those contributions to American industry possible. In whatever field you find it, but particularly in our own, it is an aristocracy of intellect, insight, and idealism. It is and must remain individualistic to satisfy those rigid requirements for greatness, enunciated so long ago.

The aristocracy of intellect is placed first because no man can serve greatly who has not an orderly, a disciplined, a trained mind. There is danger that an aristocracy of intellect can become cold, calculating, cynical, and cruel, but not if the individual belonging to it has the real elements of greatness within him, a humble searcher after truth linked with a desire to serve. Lest I be classed as a misguided visionary, let me give you the Twentieth Century Dictionary's definition of intellect: "That faculty of the human soul or mind which receives or comprehends the ideas communicated to it by the senses, or by perception, or by other means; the faculty of thinking; the understanding."

It has always been traditional with medicine that its discoveries have been widely disseminated for the good of all. The horrors of Belsen and Büchenwald, where barbaric torture and wanton destruction of helpless human lives were practiced under the guise of experimental medicine, violated every approach to intellect and descended to depths of depravity which would be almost unbelievable were not the documentary proofs so damningly convincing. Here were not orderly, disciplined, trained minds at work; minds united in a great, yet humble search for truth, but diseased and degenerated dupes of a once free profession whose very souls had been sold to the implacable hatred of a dissolute state. A cold, calculating, cynical, and cruel intellect can come only when the dignity of the individual is destroyed. Then the faculty of thinking is taken away and the understanding heart is stilled.

By contrast, one needs only to think for a moment of the contributions which a free profession made to the winning of the war and, we hope, to the preservation of the peace, to realize that the aristocracy of intellect, unhampered in the field of medicine, can literally bring men back from the jaws of death. But these lifesaving gifts were offered by a medical generation whose talents, very largely, had been developed during days of peace. This generation of physiologists, biologists, and clinicians began its work under conditions of peace. What is not so generally appreciated just now is that there has grown up a medical generation that has not had the opportunity to stimulate the intellect. They were rushed through an already crowded medical curriculum, given a few months of inadequate intern training, and sent to fill the ranks of medical officers in the Armed Services. They served courageously, and many of them died heroes' deaths. But with all honor possible given to this fine group of young men, the stubborn fact remains that we have lost a medical generation. With all due credit to the tremendous contributions that war medicine has made to the control of epidemics, the combating of shock, the prevention of wound infections, the rehabilitation of the disabled, the fact remains that our own specialty of obstetrics and gynecology has marked time. Teaching institutions lost many of their key men, as well as their residents and fellows in obstetrics and gynecology, to say nothing of their interns. Now, many of these younger men are returning from military service, eager to resume their special training

in obstetrics and gynecology. Just how heavy that load will be no one seems to know at the moment, although it has long since exceeded the ability of teaching institutions to carry it. Here is a challenge that this young association of specialists cannot and should not avoid. Some of you faculty members in our teaching centers will have to continue to work overtime to train men who can follow you; others in private practice should make places available for training by preceptorship, subject to the requirements of the American Board of Obstetrics and Gynecology. This must remain an individual problem.

We have all heard it said, repeatedly, that there are not enough specialists in obstetrics and gynecology to meet the needs of our women for specialist's care. We have also heard much about the inadequate and the uneven distribution of physicians. This is one of the arguments that has been used to force some scheme of socialization of medical practice upon us. I do not believe that the day will ever come when you will find doctors returning to the small villages of my rural State, or to any other, and I do not think that it is economically or socially sound to expect them to do so. With the advent of good roads and modern transportation, the development of adequate facilities for the care of the obstetric patient has already improved greatly in the smaller cities and in the larger towns in our rural areas. It is not necessary to subsidize or otherwise try to inveigle doctors into such areas. A proper system of preceptorships set up under conditions of free enterprise that are attractive to our thoughtful young prospective specialists will result in a more equitable distribution of those specialists in obstetrics and gynecology.

Individualism must possess or develop insight into the social, economic, and political problems that perplex the medical profession as it attempts to carry on the American tradition of free enterprise in medical practice. Emotionalism has no place in a critical approach to the sociologic problems confronting us in the practice of medicine in postwar America. We should have learned that lesson during the war years. The great shifts in population from rural to urban areas during those years, now the shift toward decentralization, have confused us. No one liked the E.M.I.C. program less than I. But the emotional outbursts against it by certain members of our profession only served to illustrate the futility of such action. The Children's Bureau, opportunely, created an emergency. That alleged "emergency" is past but I do not see that there has been any lessening of the "emergency" in the minds of those who desire a continuing bureaucratic control of the practice of obstetrics!

We have not effectively presented the case of free enterprise in obstetric practice to our patients. Our childbearing public is all through shedding tears over the heroic (?) delivery by lamplight in the kitchen of an isolated farm home. They want to know why, in a so-called modern world, such a situation should ever become necessary. This is a social problem. We have an individual responsibility to direct the social planning for the future along the constructive lines of free enterprise. If the emphasis is to be placed where I believe that it belongs, upon decentralization in government, then in the medicosocial aspects of this question we need to have the insight to direct that decentralization upon sound lines. In an imperfect society, there will probably always be those

who are indigent. Whatever the cause of their indigency, they must have medical care. The social implications of that care are tremendous. These unfortunates are the financial responsibility of the State, of you and of me as members of that State. Let us assume that responsibility by decentralizing it as much as possible for humanitarian reasons; and when local responsibility is placed, let us assume our individual responsibility by caring for the indigent mother as carefully and as conscientiously as we would care for her more socially fortunate sister. If federal funds are necessary to augment local resources in maternal care to the indigent, then let those funds be locally administered, and let us be sure that whatever local agency administers them retains and strengthens the personal relationship between patient and physician.

Individually, we must improve our political relationships if we are to develop that insight which is so necessary to our profession today. In my opinion, it is high time that we acquired political importance in matters pertaining to the health of our citizens. Such importance doesn't start in Washington. It begins in your ward and in mine. It extends onward through municipal, county, and state governments and, finally, if intelligently used, it may become effective in Congress. I have a very high regard for the Congress of the United States. I believe that, in matters of health and welfare, they are earnestly trying to work out an equitable solution to a very complex problem. How much have we helped them? Oh yes, when we have reached a sufficient degree of emotionalism regarding the E.M.I.C. program or the Wagner-Murray-Dingell Bill we have sporadically written or telegraphed them our views. But have our protests had much constructive, positive thinking back of them, or have they been largely negative? Have we had an objective approach to these great questions of maternal care, the distribution of medical care, voluntary health insurance plans, full-time health units, and many related problems? Politically and objectively these are local in origin, and we must recognize that fact and proceed accordingly if our influence is to be at all effective. We need a grass-roots organization of individualists whose constructive and objective thinking on what is best for the American mother and her baby will have political foresight and direction emanating, if you please, from our own back yards!

By some, idealism may be considered synonymous with the visionary, the fanciful, the unreal. But in individualism, as I have tried to picture it, it has a spiritual basis. This antonym of realism is what men live *for*. Without it, life becomes a long series of Tobacco Roads. Gradually it is dawning upon us that, truly, only those "things which are not seen" are eternal. *It is being driven home to men everywhere that the Sermon on the Mount is the only defense against the atomic bomb.* We move in cycles in our thinking. We have prided ourselves upon our realism in literature, the arts and industry and a "realistic approach," whatever that may be, was urged upon us in religion. But let us stop, take stock of ourselves, and see if realism and idealism have anything in common. They have, at least at one point; both search for truth. I think that we can all agree that the basic idea for the splitting of the atom, with its infinite possibilities for human destruction or for human betterment, did not originate in the minds of realists. Idealists dreamed dreams, speculated on the "sub-

stance of things not seen," worked out their mathematical formulas with a high degree of faith and, finally, on an August day in 1945, the world suddenly learned in an awful manner just a little more about a new age that had dawned. Now we know that the future of civilization rests with the idealists who will control it. This has always been true, but it will require individualists with idealism to make that future secure.

This demands an awakening of the sense of our individual responsibility to our fellow men. The idea is not new. The ancient prophet, Micah, disgusted and disheartened by the limited vision of his generation, summed it up when he said, "He hath showed thee, O Man, what is good. And what doth the Lord require of thee but to do justly and to love mercy and to walk humbly with thy God."

As we renew our annual meetings together, as we go about our daily tasks, as we face the difficult problems that lie just ahead in our social, economic, political, and professional relationships with our fellow men, let us take a large measure of idealism with us. That, with intellect and insight, will develop the individualism which is so desperately needed at this hour.

Frank Mason North, in his beautiful poem, caught the spirit of what I have been trying to say when he wrote:

Where cross the crowded ways of Life,
Where sound the cries of race and clan,
Above the noise of selfish strife,
We hear Thy voice, O Son of Man!

In haunts of wretchedness and need,
On shadowed thresholds dark with fears,
From paths where hide the lures of greed,
We catch the vision of Thy tears.

From tender childhood's helplessness,
From woman's grief, man's burdened toil,
From famished souls, from sorrow's stress,
Thy heart has never known recoil.

The cup of water given for Thee
Still holds the freshness of Thy grace;
Yet long these multitudes to see
The sweet compassion of Thy face.

O Master, from the mountain side,
Make haste to heal these hearts of pain,
Among these restless throngs abide,
O tread the city's streets again,

Till Sons of Men shall learn thy love
And follow where thy feet have trod
Till glorious from Thy heaven above
Shall come the city of our God.

In this spirit, I summon you to an individualism worth while; to the aristocracy of intellect, insight, and idealism.

MENORRHAGIA ASSOCIATED WITH IRREGULAR SHEDDING OF THE ENDOMETRIUM*†

A Clinical and Experimental Study

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WE EMPLOY the phrase irregular shedding of the endometrium to indicate a specific type of functional uterine bleeding which is characterized by prolongation of cyclic menstrual bleeding from progestational endometrium and often, in addition, by an increase in the amount of bleeding. The diagnosis is suggested by the typical clinical history of regularly recurring menorrhagia, and may be substantiated by recovering secretory endometrium by curettage during the course of the prolonged bleeding, but well beyond the time when endometrial regeneration normally would have occurred.

Although gynecologic literature contains numerous references to irregular shedding of the endometrium, this important clinical and pathologic syndrome has not been accorded the recognition it deserves. Any mention of it is noticeably lacking in the latest textbooks. We propose to show the frequency with which this diagnosis may be employed to explain menorrhagias, providing only that histologic material be obtained from the uterus at the proper time in the menstrual cycle. The characteristic clinical picture will be presented, and the microscopic findings in the endometrium will be described in detail. The results of attempts to reproduce this disorder in normally menstruating women will be shown, and a tentative explanation of the etiology of irregular shedding will be offered.

Much of the early literature has been covered adequately by Jones (1938) and also by McKelvey (1942). The earliest reference to a condition which fits our present concept of irregular shedding was that of Driessen (1914) who described prolonged and incomplete shedding of the endometrium associated with cyclic bleedings. Jones has summarized the papers of Pankow (1924), Kaufmann and Hoeck (1927), and Baniecki (1928), and it seems unnecessary to restate their contributions here. Robert Meyer (1930) included a complete description of irregular endometrial shedding in the uterine volume of the Henke-Lubarsch handbook and Rockstroh (1938), working in Meyer's laboratory in Berlin, reviewed at length the pathologic anatomy and clinical findings of what he called "delayed" shedding. He assumed that delayed shedding resulted from an insufficient production of estrin, and treated eight patients with an oral estrogenic preparation early in their menstrual cycles. The results were inconclusive. There is much to be said in favor of the use of the term

*Prize Award Essay, Clinical, presented before the Central Association of Obstetricians and Gynecologists, Fourteenth Annual Meeting, Chicago, Ill., Sept. 19-21, 1946.

†This study was aided by a grant from The Schering Corporation, Bloomfield, N. J.

"delayed," as Rockstroh has called it, rather than "irregular" shedding, and we believe that the concept of this disorder could be more readily grasped by the undergraduate medical student if some more striking term were substituted for the colorless word "irregular." While "delayed" appears to be an improvement, it obviously is not all that could be desired. However, lest we unnecessarily confuse the picture even before this diagnosis is widely established, we have decided against any attempt to improve upon the term previously employed by the vast majority of investigators.

In this country numerous papers have dealt with the subject of functional uterine bleeding, but few have been concerned with endometria exhibiting the characteristics of irregular shedding. Traut and Kuder (1935) described both irregular or incomplete shedding, an aberration of the secretory phase of the cycle, and irregular ripening or maturation, representing a mixture of both proliferative and secretory phases. Irregular ripening was characterized by bleeding in the midportion of the menstrual cycle (metrorrhagia) and the endometrium suggested a patchy or irregular corpus luteum effect superimposed upon the proliferative phase. We have not encountered metrorrhasias presenting this particular histologic picture, and we are at least mildly skeptical concerning the reality of such a clinical entity since we have made an earnest endeavor to classify by histologic means every patient relating any derangement of the menstrual cycle. Traut and Kuder emphasized that irregular shedding and irregular ripening had been neglected by students of uterine bleeding although in their experience these disorders accounted for approximately one-third of all functional uterine bleeding. Hamblen (1939, 1945), recognizes that abnormal bleeding (menorrhagia) can occur from progesterational endometria, but he has not seen fit to dignify this situation with a specific diagnostic title. In his monographs he refers briefly to irregular shedding of the endometrium, but considers it a minor variation of normal menstruation. Jones (1938) discussed functional uterine bleeding associated with secretory endometrium, but concluded that the patients studied had "no characteristic menstrual history" and that the endometrium of irregular shedding, as described by others, had no peculiarities which would allow it to be set apart as a pathologic entity. Wilson and Kurzrok (1938) made brief mention of Traut's "irregular ripening," but decided to exclude any such disorder from their concept of mixed endometria. Apparently they were not at all impressed by the possible importance of irregular shedding. Strangely enough, these investigators had never encountered an endometrial section which suggested the persistence of an actively secreting corpus luteum beyond a period of fourteen days. Israel and Mazer (1938), on the other hand, were prepared to admit that irregular shedding of the functional layers of the endometrium might be the immediate cause of prolonged or excessive bleeding. Mann and his associates (1942) indicated a familiarity with Traut's description of irregular shedding but, for reasons which were not disclosed, felt that such an entity could not be fitted into any physiologic or pathologic scheme "except by some tortured interpretation."

In 1940, Sturley reviewed an experience with seventeen cases of irregular shedding seen at the University of Minnesota Hospital. Two years later McKelvey (1942) presented a brief general survey of the problem and a preliminary report on 36 patients observed in the same clinic. Recently Professor McKelvey has very kindly permitted us to read in manuscript form a paper dealing extensively with the same material. With minor exceptions, his observations have paralleled our own as set forth below. He suggests that the pathologic findings in the endometrium may be linked in some way with persistence through more than one menstrual cycle of thick-walled spiral arterioles. His urinary

excretion studies, carried out in six cases, indicated that pregnandiol was excreted during the menstrual bleeding, contrary to the usual finding, and from this it was inferred that irregular shedding might be a specific endocrinologic entity.

The Histology of Normal Menstruation

We employ the term menstruation to designate uterine bleeding associated with the shedding of an endometrium which has manifested secretory or progestational changes. To justify our contention that irregular shedding of the endometrium is an abnormal condition, a brief review of the events in normal menstruation seems desirable at this point. The various aspects of menstruation have been covered exhaustively by Schroeder (1928), R. Meyer (1930),



Fig. 1.—Curettage material obtained on the fifth day of normal cycle. Surface reformed, glands in early proliferation stage.

and Bartelmez (1937, 1941). The corpus luteum presumably ceases to function one or two days before the onset of menstruation, and, consequently, the excretion of pregnandiol, formed from progesterone, terminates with the appearance of bleeding. The vascular changes appearing in the spiral arteries of the functionalis at the beginning of menstruation have been observed in vivo on ocular transplants in the Macaque by Markee (1940). Constriction of these vessels occurs twenty-four hours before the appearance of hemorrhage. There is marked blanching of the mucosa, a reduction in size of the transplant, then arteriolar dilatation and extravasation of blood. Hematomas form, and finally bits of tissue become detached from the surface in regions where hemorrhage has occurred.

While bleeding from the human uterus at the time of normal menstruation ordinarily lasts from four to seven days, there is rather general agreement that the actual shedding of endometrial tissue is complete within two to four days. Novak and TeLinde (1924), after examining uteri removed during menstruation, concluded that shedding was very extensive by the second day, and regeneration of surface epithelium from stumps of uterine glands was conspicuous on the third day. More recently, Novak (1940) has set the third day as the time when desquamation has commonly reached its limit. Bartelmez (1933), in a study of 17 surgical specimens subjected to immediate fixation, described and illustrated endometrial repair appearing early on the fourth day after the onset of menstrual bleeding. Herrell and Broders (1935) stated "there can be no doubt that loss of tissue is complete in the first twenty-four hours of menstruation, and that the remainder of the menstrual period is one of hemorrhage and secretion." Campbell and his associates (1936) also concluded that the stage of tissue loss is brief, lasting not more than one or two days, and that before it is completed re-epithelization has already begun.

From these observations, and on the basis of our own studies of normally menstruating women, it would seem reasonable to conclude that the shedding of secretory tissue ordinarily is completed within forty-eight to seventy-two hours after the onset of bleeding. Regeneration of a new surface occurs rapidly thereafter, and by the fourth or fifth day of the cycle one almost routinely observes new proliferative endometrium. Fig. 1 shows a section of endometrium obtained by curettage from a 22-year-old normal woman who had a regular cycle of twenty-five to twenty-eight days, with bleeding lasting five to six days. Curettage was done on the fifth day of bleeding. Note complete regeneration of the surface epithelium and early proliferation changes in the glands.

We should not expect to find on the fifth day of menstruation comparatively large areas of secretory glands belonging to the previous cycle. This finding, coupled with a characteristic clinical history of menorrhagia, has been our criterion for the diagnosis of irregular shedding of the endometrium.

Pathology

The salient pathologic feature of the disease is that the endometrium remains in menstrual decomposition over a prolonged period of time. As mentioned above, in the normal cycle the shedding of the menstrual endometrium is usually completed in two days, and regeneration of the surface epithelium is complete by the fifth day. In the typical case of irregular shedding of the endometrium, the process of shedding will still be occurring on the fifth day of bleeding or even later. In order to make the diagnosis, curettage material must be obtained at the time when it will show the most characteristic findings, namely, on the fifth or sixth day of bleeding. Also, the pathologist must interpret the findings in relation to the menstrual history. Endometrium obtained on the first day of a normal cycle will show many of the characteristics of endometrium obtained from a case of irregular shedding on the fifth day. Failure to appreciate this fact has, we believe, been the chief obstacle to a wider recognition of the disease process. Endometrium obtained at the proper time in the cycle will show the following characteristic findings: There is marked irregu-

larity in the thickness of the endometrium. The surface epithelium is missing. The stroma is shrunken and composed of many deeply basophilic nuclei with little cytoplasm. The glands are collapsed but show evidence of secretion change. Most of the secretion of the cells has been discharged. The lumina appear star-shaped when cut in cross section as a result of collapse and shrinkage of the surrounding stroma. Many arterioles near the surface are dilated and have a thicker wall than is usually seen in this portion of the endometrium. These points will be stressed again in the presentation of the clinical material below.

In the interpretation of this material, it must be borne in mind that these areas of endometrium belong to the previous cycle. Although retained for abnormally long periods of time, the tissue is gradually cast off. The normal mechanism of regeneration is continuing through this period in an irregular fashion, and is apparently able to catch up before the next ovulation occurs in at least a large proportion of the endometrium. Therefore there is usually no change in the length of the cycle over the normal.

Clinical Material

During a period of three years, uterine curettage was carried out on 242 patients in the Salt Lake General Hospital. A pathologic diagnosis of irregular shedding of the endometrium was made in 22 of these. The diagnosis was also made in several additional instances, but the bleeding abnormality in these cases was so closely associated with a recent abortion that these were thought to be more properly labeled as postabortal subinvolution of the endometrium, and are therefore not included in the present report. This was substantiated in follow-up studies of the postabortal cases, all of whom had no recurrence of the bleeding abnormality following curettage, whereas many of the cases of true irregular shedding had no relief from curettage or were ultimately treated by surgical intervention. A breakdown of the 22 cases from a standpoint of age incidence, parity, duration of bleeding, and length of the cycle is of interest.

TABLE I. AGE INCIDENCE

20 to 30 years	11 cases
30 to 40 years	8 cases
40 plus years	3 cases

TABLE II. PARITY

0	2 cases
1-11	20 cases

This is of particular interest in view of the fact that previous authors have reported the highest incidence of the disease near the age of the menopause. The cases which have proved to be the most refractory to treatment and which have posed the most difficult problems in our experience have been those in the early age group. Three such cases will be discussed in detail below.

The preponderance of cases in women who have had pregnancies cannot be overlooked as a possible clue to etiology. In half of our cases, the patients also dated the onset of the abnormal bleeding to a pregnancy.

TABLE III. DURATION OF BLEEDING

7 to 9 days	6 cases
10 to 15 days	15 cases
Over 15 days	1 case

TABLE IV. LENGTH OF MENSTRUAL CYCLE

Less than 25 days	4 cases
25 to 30 days	11 cases
Over 30 days	7 cases

Any statement as to duration of bleeding is of necessity an approximation, for many times there was a variation of as much as four days from period to period. Some criticism might be leveled at designating a period of bleeding lasting seven days as prolonged. Nevertheless, the increase of length of flow up to seven days represented a distinct change in the menstrual habits of these patients, and prompted them to seek medical advice because of the change.

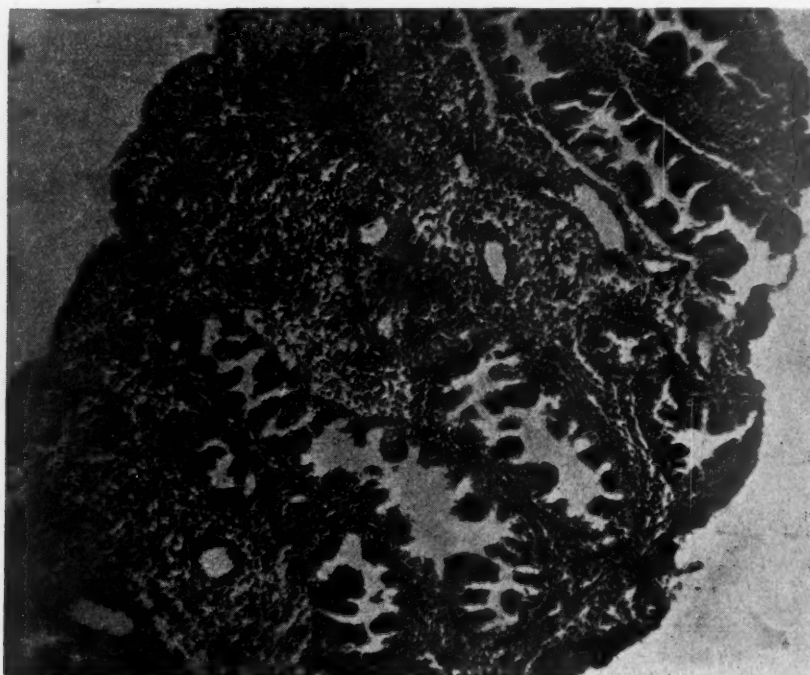


Fig. 2.—Case 1. Endometrium removed on sixth day of bleeding, showing marked retention of secretory glands, overdevelopment of stroma.

There seems to be no correlation between the duration of bleeding and the length of the menstrual cycle. One patient, who had periods of bleeding lasting fifteen to twenty days out of each cycle, still could predict the onset of her next bleeding, and the cycles were thirty days in length. Another patient, who had periods of bleeding lasting twelve days, had a cycle which was regularly twenty-four days in length.

Space does not permit a discussion of all of the cases which make up the material for this report. In order to demonstrate the nature of the problem, three cases will be reported in detail and microscopic sections from five additional cases will be shown.

CASE 1.—M. S. (Hosp. No. 8362), aged 25 years, para ii, was first seen in January with the complaint of prolonged periods of vaginal bleeding since the birth of her last child three years previously. Cycles were regular every 28 to 32 days, but flow was very profuse and lasted for fourteen days. Last period of bleeding before admission was from December 22 to January 4. Pelvic examination revealed no abnormalities. Curettage was carried out on the sixth day of the next bleeding which began on January 23. Examination of the curettage material showed marked retention of the secretory phase endometrium from the previous cycle (Fig. 2). The next period of bleeding began on February 25. Endometrial biopsy was obtained on the fifth day of bleeding.

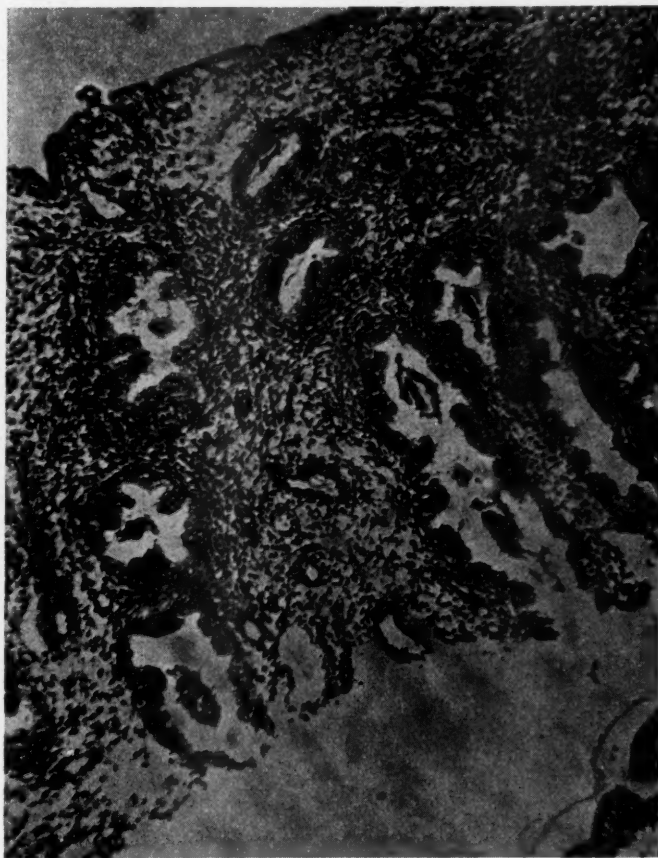


Fig. 3.—Same case as Fig. 2. Endometrium removed on fifth day of next menstrual cycle.

Examination of this tissue showed a picture similar to that obtained by curettage (Fig. 3). Bleeding continued for an additional nine days after the biopsy was taken. Pelvic examination on April 7 revealed the presence of a 6 cm. cystic mass in the region of the left ovary. This was thought to represent a follicle cyst of the ovary. On the eighth day of the last bleeding a subtotal hysterectomy was carried out, together with removal of the left ovarian cyst, which proved to be only a cystic follicle. Sections through the uterine wall showed scattered areas of adenomyosis. The endometrium again demonstrated delay in shedding and lack of healing of the surface even though the uterus was removed on the eighth day of bleeding (Fig. 4).

CASE 2.—V. J. (Hosp. No. 2117), aged 23 years, para ii. First seen in September, at which time she complained of prolonged periods of vaginal bleeding for the preceding three months. Her last pregnancy was two years previously. Menses occurred at intervals of thirty days, but flow was prolonged up to fifteen to twenty days. Previously, flow had never been more than six days in duration. Physical examination and workup revealed no abnormalities aside from an anemia with a hemoglobin value of 10 grams. Pelvic examination revealed apparently normal internal genitals. Dilatation and curettage was done on the seventh day of bleeding. The endometrium showed an excessive secretory change in the glands, marked delay in the shedding of the endometrium, and overdevelopment of the stroma (Fig. 5). Bleeding continued for four days following the curettage. The patient was readmitted two months later with the same complaint. Bleeding period during the interim had lasted for fifteen days.

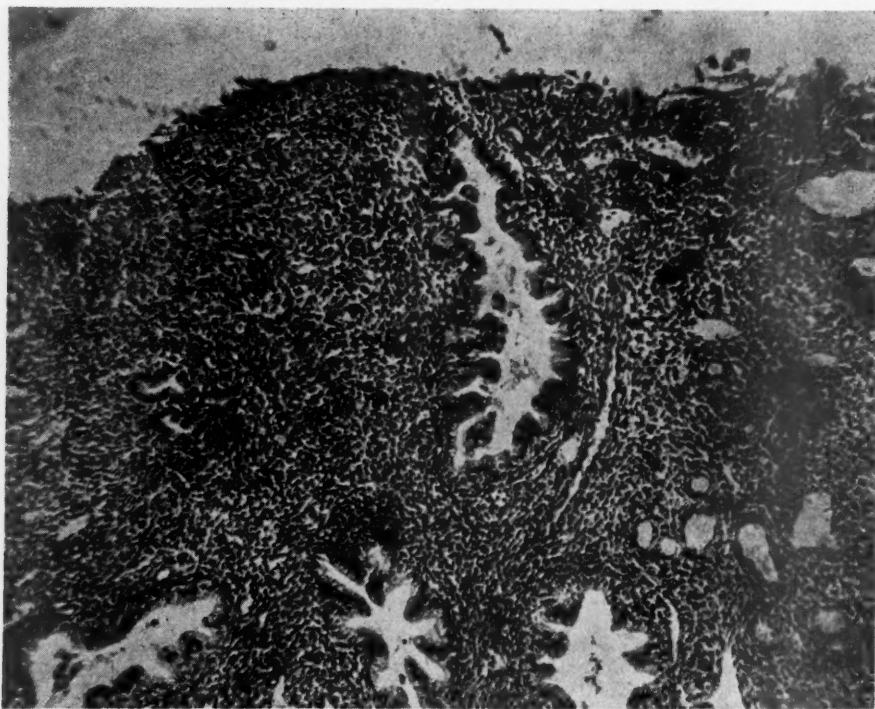


Fig. 4.—Same case as Figs. 2 and 3. Endometrium from hysterectomy specimen obtained on eighth day of bleeding, showing retention of secretory glands, delay in healing of surface.

At the time of admission in November she had already been bleeding for ten days. The endometrium showed marked delay in regeneration. Remnants of old secretory glands from the previous cycle could still be recognized (Fig. 6). The patient was readmitted again on February 11. Bleeding periods meanwhile had been as follows: December 8 to 28; January 6 to 21; February 4 to admission. Beginning on January 29 (twenty-fourth day of last cycle) the patient was given daily intramuscular injections of 10,000 units of estrogenic hormone in oil in an attempt to control the bleeding. This was continued for the next nine days (three days after the onset of bleeding) and was found to have no apparent effect on the amount or duration of the bleeding. On February 13 (tenth day of bleeding) subtotal hysterectomy was carried out. No gross abnormalities were found either in the uterus or the appendages. Sections taken

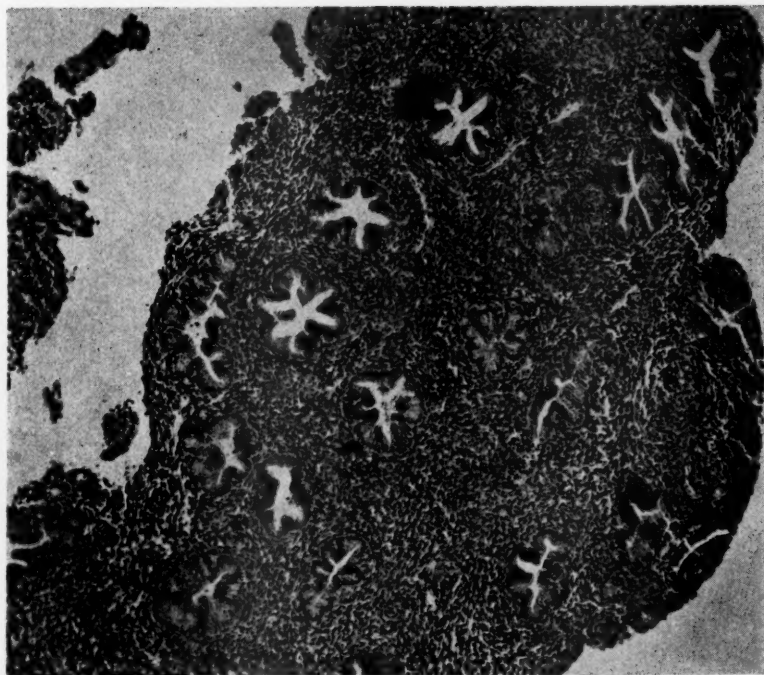


Fig. 5.—Case 2. Endometrium obtained on seventh day of bleeding showing retention of secretory glands which are collapsed, compact stroma.

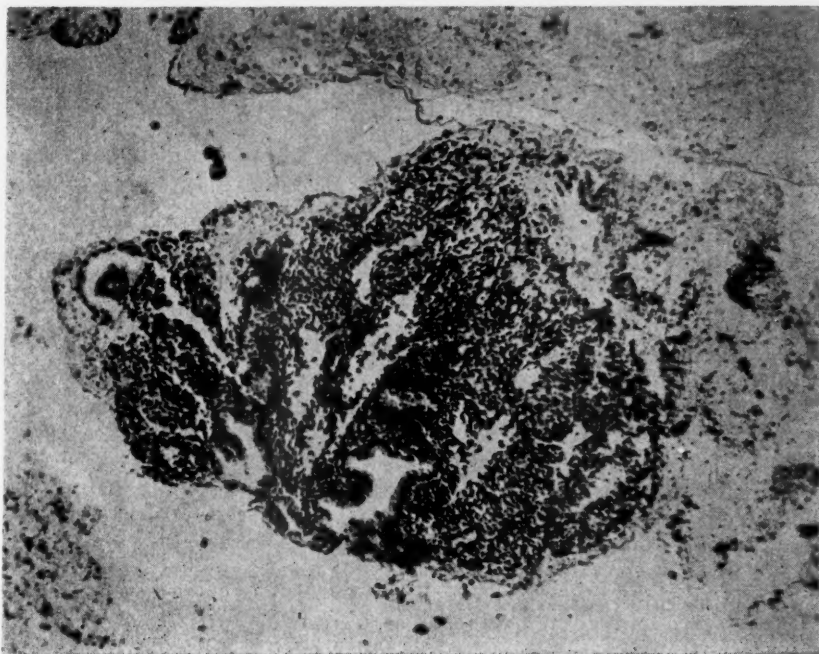


Fig. 6.—Same case as Fig. 5. Endometrium obtained on tenth day of bleeding showing retained secretory glands, delay in regeneration.

through the uterus again showed a delay in the shedding of the endometrium from the previous cycle and little evidence of regeneration. Large blood vessels, some of which were thrombosed, could also be seen on the endometrial surface (Fig. 7).

CASE 3.—J. H. (Hosp. No. 1679), aged 31 years, para vii, was first seen in January. She stated that her periods had been regular and lasted for six days up to birth of her last child in the previous February. Since that time menses had continued to recur at intervals of twenty-four days, but flow was prolonged up to 12 days. Examination on admission showed presence of a chronic anemia (hemoglobin 11 grams), splenomegaly and hepatomegaly, no pelvic abnormalities.

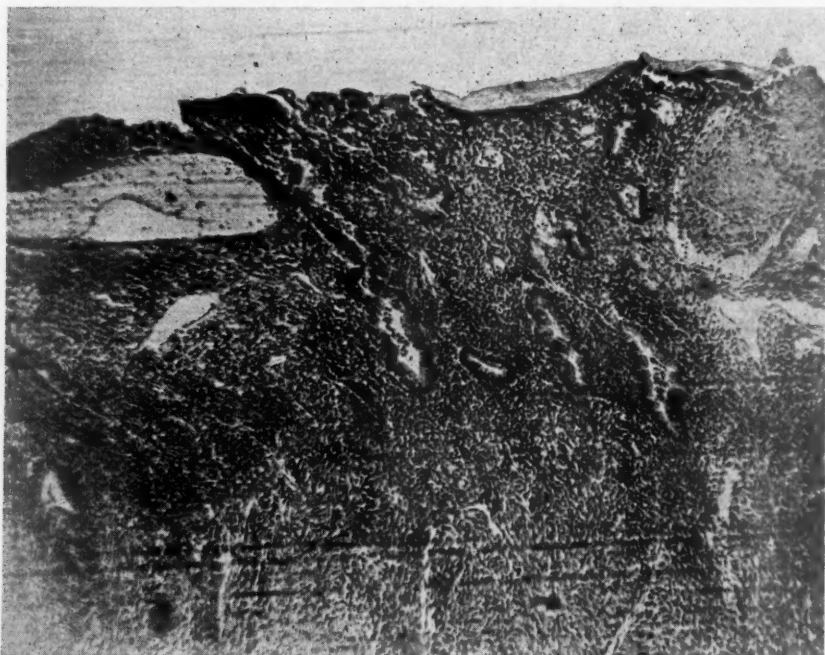


Fig. 7.—Same case as Figs. 5 and 6. Endometrium from hysterectomy specimen obtained on tenth day of bleeding. There is delay in endometrial growth. Note large thrombosed vessel near the surface.

Complete workup by the Department of Internal Medicine indicated that the splenomegaly and hepatomegaly were associated with the hypochromic anemia which was thought to be due to chronic blood loss. Curettage was done on the fifth day of bleeding. The endometrium showed retention of secretory glands from the previous cycle, delay in healing of the surface, and the presence of large blood vessels in close proximity to the secretory glands (Fig. 8). The patient was readmitted in July with the same complaints. Since the previous curettage, the patient had continued to bleed at intervals of twenty-four to twenty-six days with profuse periods of bleeding lasting ten to twelve days. Curettage was repeated on the sixth day of bleeding. The endometrium showed a similar picture to that obtained previously (Fig. 9). Patient was readmitted for the third time in December, 1945, with the same complaints. The anemia had not responded to therapy. Hemoglobin on admission was 8.8 grams. The Department of Internal Medicine urged that hysterectomy be carried out in order to cure the anemia. A subtotal hysterectomy was carried out on the twenty-



Fig. 8.—Case 3. Endometrium obtained on fifth day of bleeding showing secretory glands from previous cycle, large blood vessels in close proximity to secretory glands.

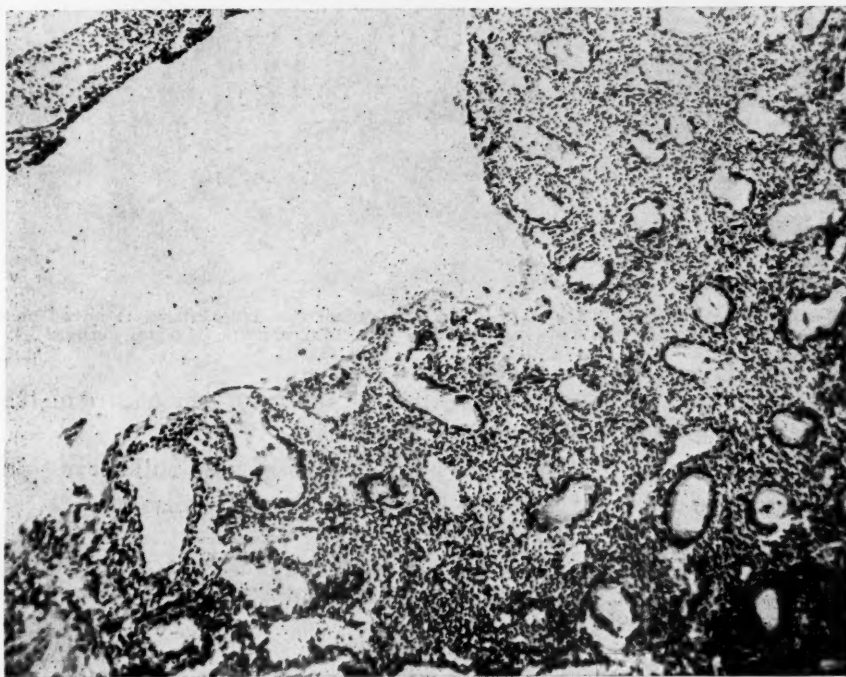


Fig. 9.—Same case as Fig. 8. Endometrium obtained on sixth day of bleeding showing delay in healing of the surface, numerous secretory glands from previous cycle.

second day of the cycle. Grossly, the uterus and appendages presented no abnormalities. Microscopic section of the endometrium showed an excessive degree of secretory change. Even the basal glands in direct contact with the myometrium showed progesterone effect (Fig. 10). This could perhaps indicate an excessive progesterone stimulation which might have an etiologic significance. This possibility is described more fully below. The anemia cleared completely following cessation of the menstrual bleedings.

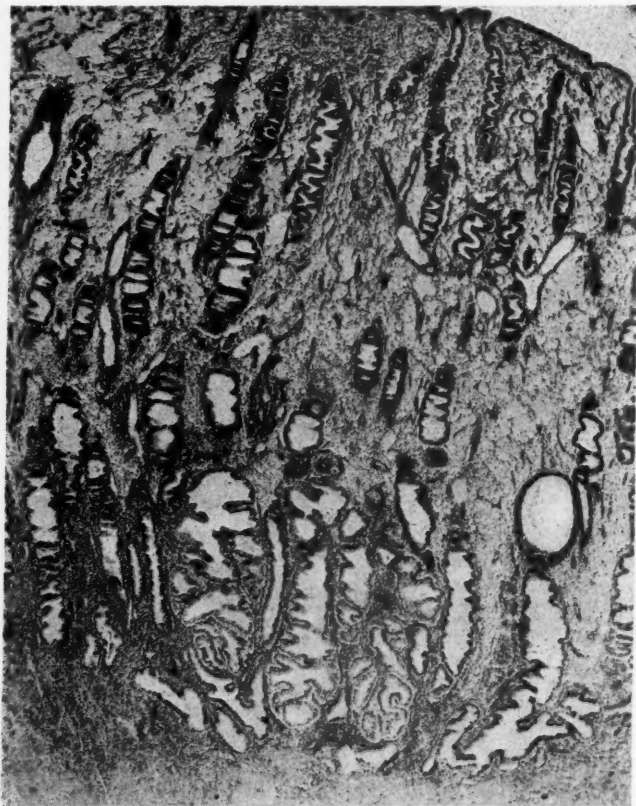


Fig. 10a.—Same case as Figs. 8 and 9. Section of endometrium from uterus removed on twenty-second day of cycle, showing excessive secretory change in basal glands.

The three cases presented all demonstrate the recurrent nature of the problem. None of these cases benefited from curettage.

Less detailed presentation of an additional five cases will serve to demonstrate further the characteristic histologic features of the disease.

CASE 4.—A. M. (Hosp. No. 6598), aged 38 years, para iv. Complaint: bleeding fourteen days out of each twenty-eight-day cycle. Curettage done on fifth day of bleeding (Fig. 11).

CASE 5.—I. H. (Hosp. No. 9043), aged 45 years, para ii. Complaint: bleeding for twelve days out of each twenty-one- to twenty-four-day cycle. Curettage on fourth day of bleeding (Fig. 12).

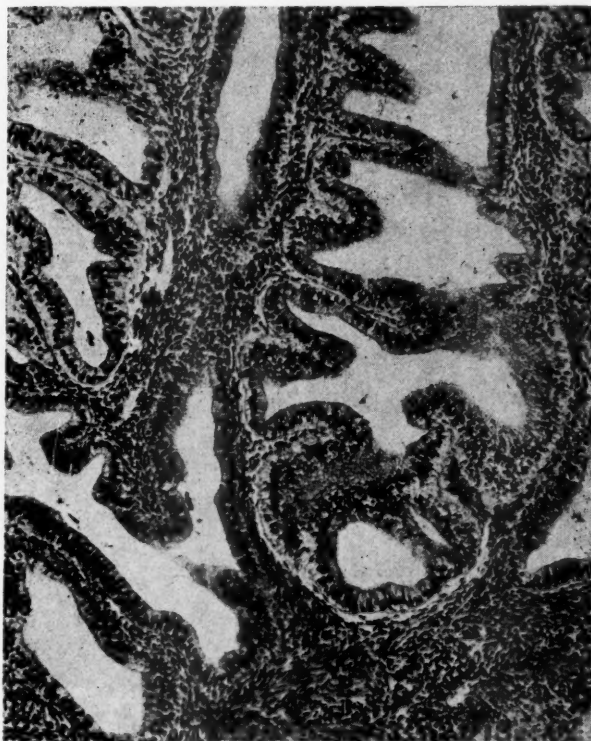


Fig. 10b.—High-power view of basal glands in Fig. 10a. Note marked evidence of progesterone effect on basal glands.

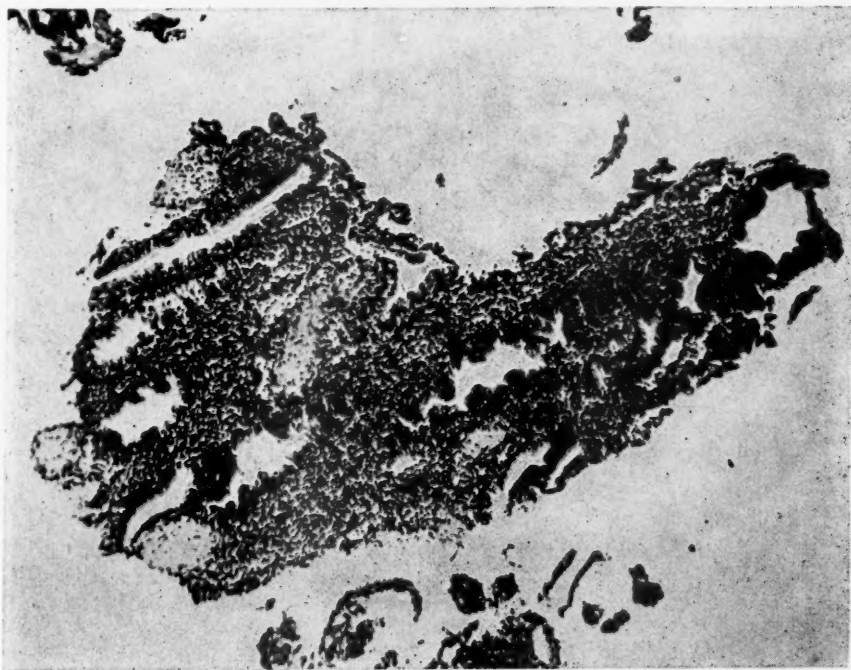


Fig. 11.—Case 4. Endometrium obtained on fifth day of bleeding showing presence of secretory glands from previous cycle, delay in healing of surface, thrombosed vessels.

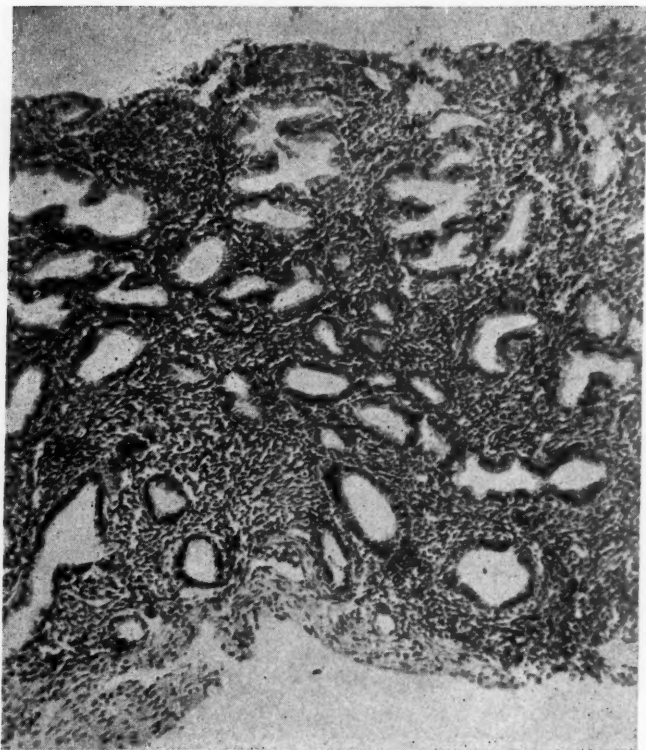


Fig. 12.—Case 5. Endometrium obtained on fourth day of bleeding, showing absence of surface epithelium, retention of secretory glands.

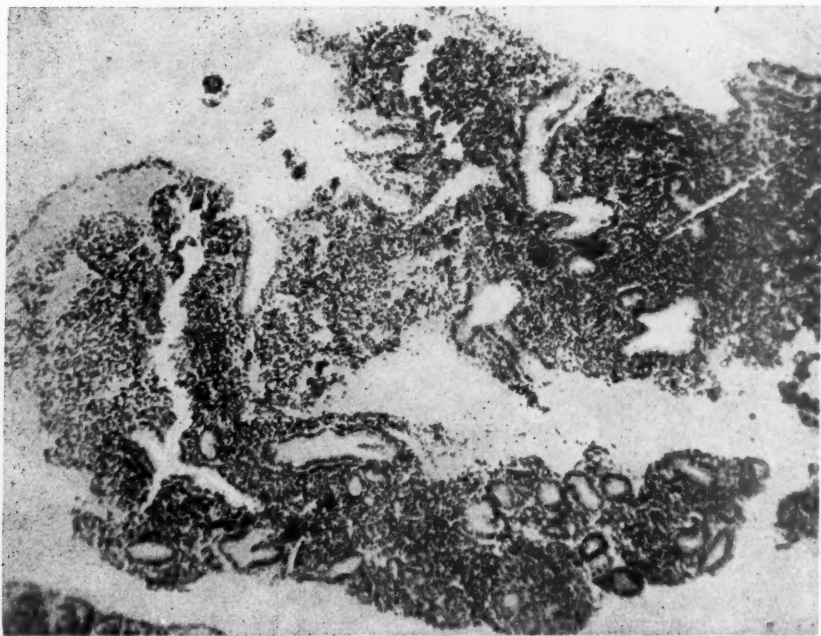


Fig. 13.—Case 6. Endometrium obtained on fifth day of bleeding showing retention of secretory glands.

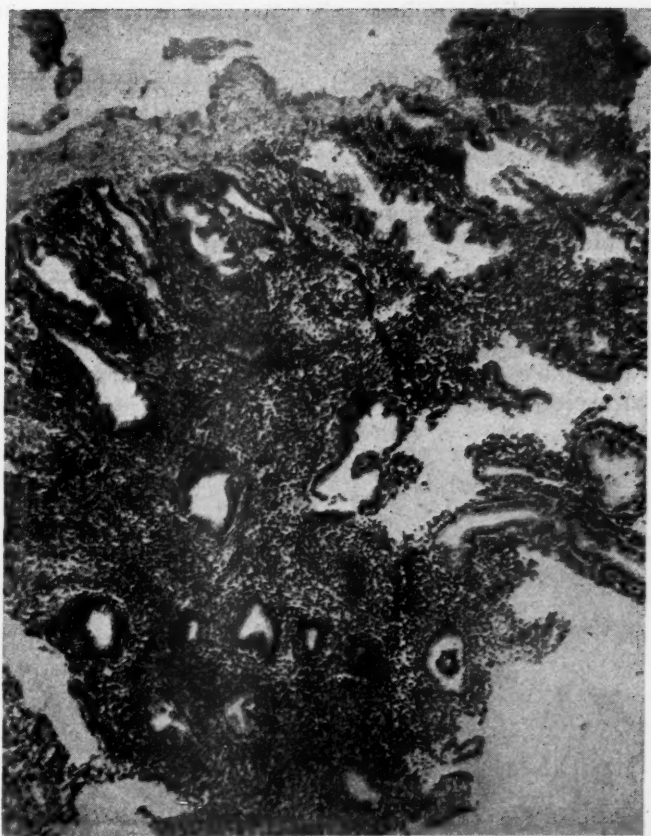


Fig. 14.—Case 7. Endometrium obtained on sixth day of bleeding, showing delay in surface healing, retained secretory glands.

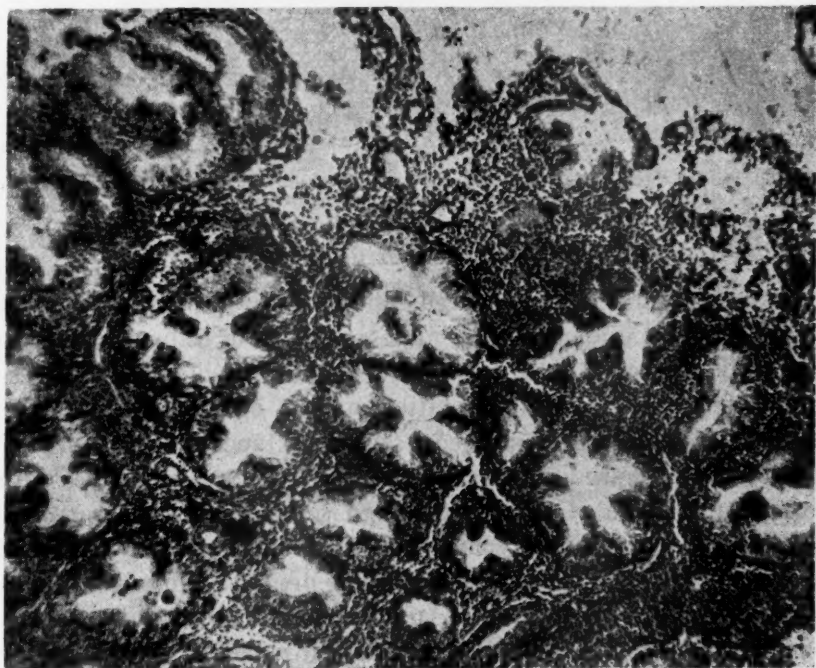


Fig. 15.—Case 8. Endometrium obtained on third day of bleeding. The large, collapsed secretory glands show excessive progesterone effect.

CASE 6.—M. B. (Hosp. No. 4688), aged 32 years, para iii. Complaint: bleeding nine days out of each thirty-day cycle. Curettage on fifth day of bleeding (Fig. 13).

CASE 7.—H. F. (Hosp. No. 3870), aged 30 years, para v. Complaint: bleeding for ten to fourteen days out of each thirty-day cycle. Curettage done on sixth day of bleeding (Fig. 14). This patient eventually had hysterectomy performed. The uterus showed the presence of adenomyosis.

CASE 8.—G. P. (Hosp. No. 8392), aged 23 years, para i. Complaint: bleeding for fourteen days out of each twenty-eight to thirty-day cycle. Curettage done on third day of bleeding (Fig. 15). Endometrial biopsy taken on fifth day of next cycle (Fig. 16).



Fig. 16.—Same case as Fig. 15. Endometrial biopsy taken on fifth day of next cycle shows retention of secretory glands.

Etiology and Experimental Study

There are a number of associated lesions in the uterus and endometrium which may play an etiologic role. The presence of submucous myomas or endometrial polyps may interfere with the normal shedding process. The association of postabortal subinvolution of the endometrium and irregular shedding has already been mentioned. The simultaneous occurrence of adenomyosis and irregular shedding, as demonstrated in two of our cases, may be indicative of a common etiology of the two conditions. However, after these etiologic possibilities have been considered, there still remain a large number of cases in which the etiology is obscure. Our present study is concerned particularly with this group of cases. An attempt has been made to demonstrate a hormonal basis for these. From a theoretical standpoint it would seem that the corpus luteum and its hormone progesterone should play an important

role inasmuch as the outstanding feature of the disease is failure of the uterus to shed endometrium which has undergone progesterone stimulation. This failure may be due to prolonged stimulation of the endometrium by progesterone, i.e., failure of the corpus luteum to undergo prompt and complete regression just prior to menstruation. On the other hand, the defect may be primarily in the endometrium itself, i.e., for some unknown reason there is failure of the endometrium to shed promptly due to an inherent deficiency in the endometrium or its vascular bed. The process of menstruation is inseparably tied up with the blood supply to the endometrium. If the process of constriction of the spiral arterioles and subsequent ischemia is interfered with, it is easy to see how this might influence the normal process of shedding and produce the clinical picture which is so characteristic of irregular shedding of the endometrium.

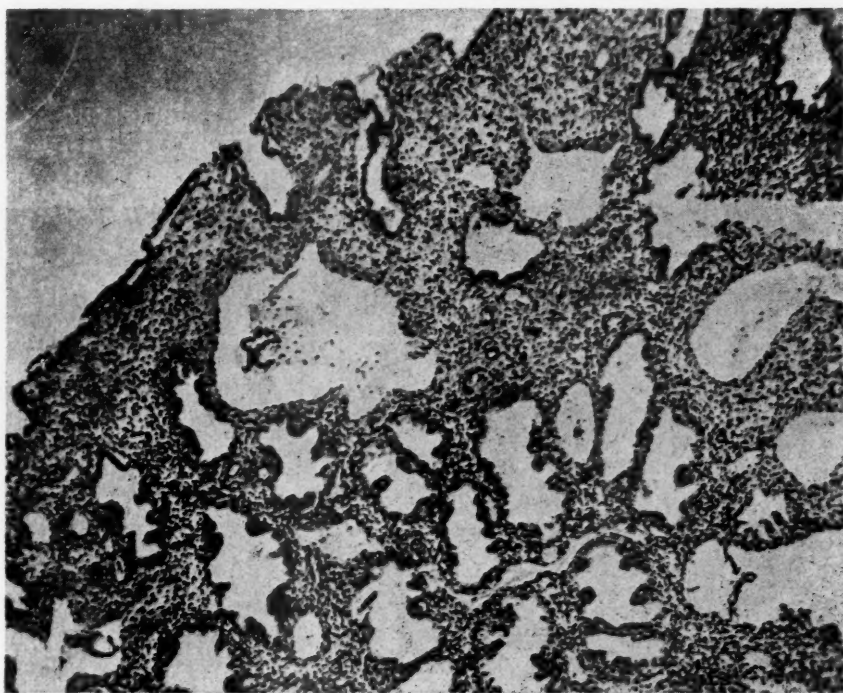


Fig. 17.—Experimental case 1. Endometrium obtained on sixth day of bleeding following administration of 30 mg. of progesterone daily beginning on first day of bleeding. The surface epithelium is intact, and the secretory glands from the previous cycle have not been shed.

The hormonal theory of etiology offers the best opportunity for experimental study. Investigation thus far has been along these lines. Some indication of corpus luteum activity can be obtained by the study of urinary excretion of pregnandiol. Previous investigators have reported the presence of this substance in the urine during the last half of the cycle, with an abrupt drop in the excretion twenty-four to forty-eight hours before the onset of menstruation, paralleling the activity of the corpus luteum. In the normal cycle there is no significant excretion of pregnandiol in the urine during the bleeding phase.

Some studies on patients exhibiting irregular shedding of the endometrium have indicated that they do not follow the normal pattern of pregnandiol excretion, but continue to excrete the substance during the bleeding phase. We have

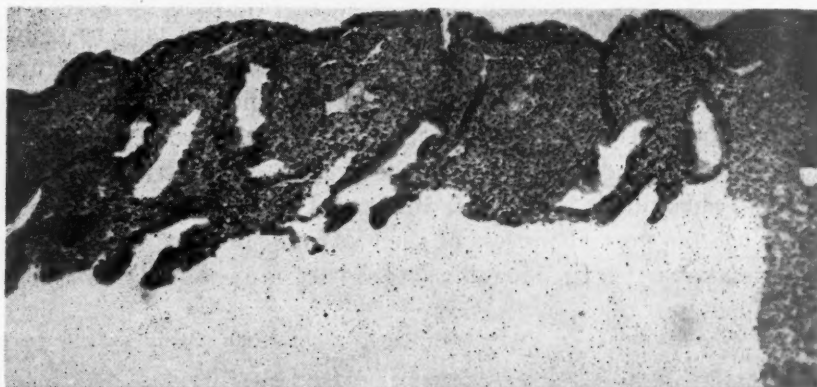


Fig. 18.—Experimental case 2. Endometrium obtained on the fifth day of bleeding after administration of 10 mg. of progesterone daily beginning on twenty-fourth day of cycle. Bleeding began on the thirty-first day. The glands are in the secretion phase and the stroma has a deciduallike appearance.

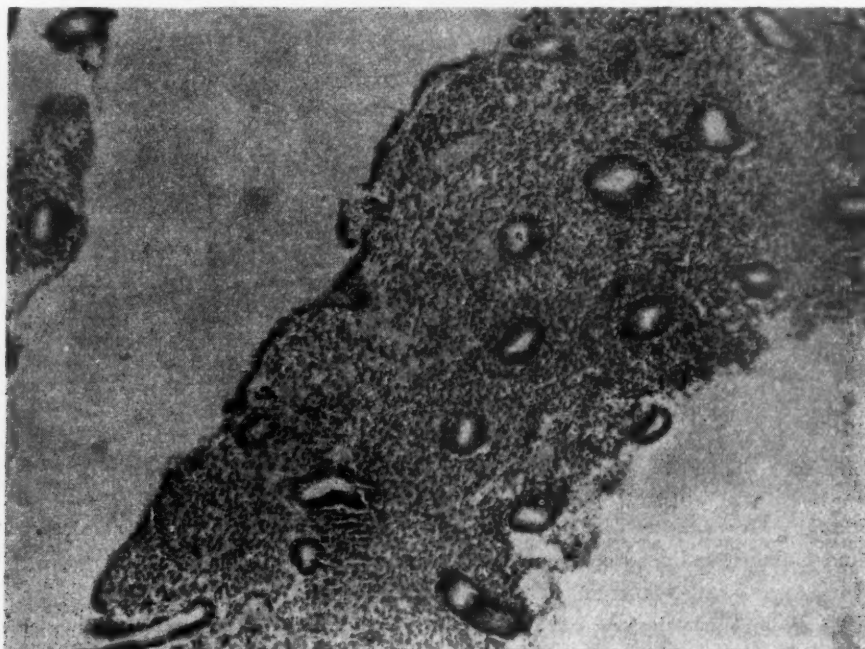


Fig. 19.—Experimental case 3. Endometrium obtained on fifth day of bleeding. Beginning on twenty-sixth day of cycle, 20 mg. of progesterone was administered daily until onset of bleeding, which was delayed until thirty-seventh day of cycle. Progesterone was then discontinued. There is no retention of secretory glands, or apparent delay in shedding.

tried to confirm these findings in a small group of cases, but our results have not been consistent enough to draw any conclusions. This investigation is being continued at the present time.

If the hypothesis of prolonged progesterone effect be correct, it should be possible to reproduce the disease in the normal patient by administering progesterone during the bleeding phase of the cycle. We have attempted to do this with interesting results.

EXPERIMENTAL CASE 1.—V. W., aged 16 years, para 0, presented no gynecologic complaints. Menses were regular every thirty days with a four- to five-day flow. Recent periods of bleeding before administration of hormone were as follows: February 22; March 23; April 18. As soon as bleeding was noted on April 18, injections of progesterone were started. Thirty milligrams of progesterone in oil were administered daily for the next six days, during which time bleeding continued in small amounts. On the sixth day after the onset of bleeding, curettage was carried out. A large amount of endometrium was obtained, a typical section of which is shown in Fig. 17. The surface epithelium is intact, the glands show marked secretory change, and the stroma is overdeveloped. This picture is similar to that seen in the endometrium removed from our clinical case 1 (Fig. 2).

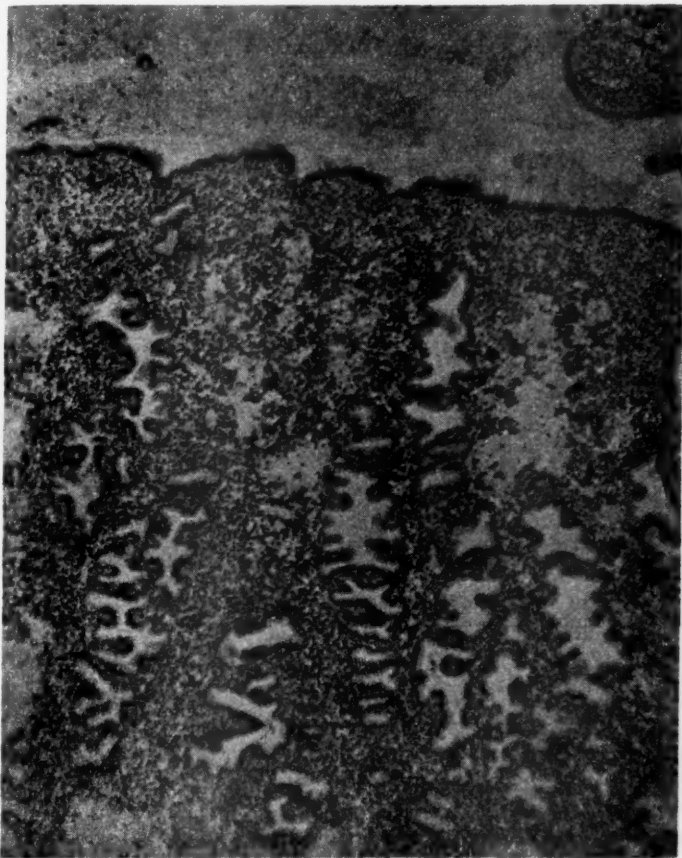


Fig. 20.—Experimental case 4. Endometrial biopsy taken on thirty-sixth day of cycle after administration of progesterone beginning on twenty-sixth day of cycle.

EXPERIMENTAL CASE 2.—R. M., aged 23 years, para 0. No gynecologic complaints. Menses occurred every twenty-six to twenty-eight days. Beginning on the twenty-fourth day of the cycle the patient was given 10 mg. of progesterone daily. Bleeding began on the thirty-first day of the cycle.

Progesterone was continued in the same dosage until the fifth day of bleeding, at which time curettage was done. Microscopic section of curettage material showed evidence of retention of the secretory endometrium as in the previous case (Fig. 18).

EXPERIMENTAL CASE 3.—V. M., aged 30 years, para 0, presented no gynecologic complaints. Menses were regular, with a twenty-eight-day cycle. Last menstrual period had been January 26; expected next menses was about February 24. Beginning on February 20 (twenty-sixth day of cycle) patient was given 20 mg. of progesterone daily. This was continued until the onset of bleeding which was delayed until March 3 (thirty-seventh day of cycle). Progesterone was then discontinued. Curettage was carried out on the fifth day of bleeding. Sections showed normal regeneration phase endometrium (Fig. 19).



Fig. 21.—Same case as Fig. 20. Endometrium obtained on fifth day of bleeding after continuation of progesterone administration into bleeding phase. Note delay in shedding and regeneration.

EXPERIMENTAL CASE 4.—E. D., aged 36 years, para 0, presented no gynecologic complaints. Menses occurred every twenty-eight to thirty days. Her last menstrual period had been February 5, and expected next menses about March 5. Twenty milligrams of progesterone were administered daily beginning on March 2 (twenty-sixth day of cycle). Dose decreased to 10 mg. daily beginning on thirty-third day of cycle when bleeding had failed to occur. This dosage was continued daily until four days after bleeding had begun (thirty-eighth day of cycle). Endometrial biopsy was taken on thirty-sixth day of the cycle. This showed a markedly excessive secretory change in the endometrium (Fig. 20). Curettage was done on the fifth day of bleeding. Section showed beginning evidence of regeneration of the surface and less retention of secretory endometrium than in case 1 (Fig. 21). Note that the dose of progesterone in this case was only 10 mg. daily, as compared with 30 mg. used in case 1.

These studies would seem to indicate that at least the microscopic picture which we recognize as characteristic of irregular shedding of the endometrium can be reproduced in the normal patient by administration of proper doses of progesterone during appropriate phases of the cycle. Apparently progesterone must be administered during the bleeding phase in order for the secretory endometrium to be retained. Administration of progesterone in dosage of at least 20 mg. daily during the last portion of the cycle will delay the onset of menstruation. However, there appears to be a critical level above which bleeding can be prevented indefinitely from occurring. In our cases this seemed to require a dosage of between 20 and 30 mg. of progesterone daily. A dosage of 10 mg. daily did not prevent menstruation from occurring, but the expected period was delayed in its onset. The endometrium will be shed in the usual period of time unless progesterone is continued in a dosage of at least 20 mg. daily during the bleeding phase. In none of the experimental cases was bleeding profuse when it did occur. Whether or not bleeding would have been prolonged will have to be determined by future studies in which the patient is allowed to bleed without curettage having been performed.

Treatment

At the present time no recommendation as to treatment can be made. Previous authors have stressed the fact that curettage alone acts as a therapeutic as well as a diagnostic procedure. Our experience has not been so fortunate. Reference has been made to three cases finally treated by hysterectomy after repeated curettage had failed to be of therapeutic value. Administration of estrogenic substance during the bleeding phase might be expected to speed up the process of regeneration. This type of therapy was tried out on three of our patients without noticeable effect either on the amount or the duration of the bleeding. One patient who was ultimately subjected to hysterectomy felt that the estrogen therapy made the bleeding more profuse. We feel, however, that this form of therapy has not received an adequate test and should receive further trial. In the menopausal group, sterilization by irradiation is the treatment of choice.

Summary and Conclusions

1. Cyclical menorrhagia is frequently caused by irregular shedding of the endometrium.
2. Irregular shedding of the endometrium is a clinical and pathologic syndrome characterized by a typical pathologic picture, the outstanding feature of which is prolongation of shedding of the endometrium which has undergone progesterone stimulation.
3. The diagnosis depends upon correlation of the endometrial pattern with the menstrual history. Knowledge of the menstrual history is essential for a histologic diagnosis.
4. During the nonbleeding phase of the cycle the endometrium may be normal.

5. Diagnostic curettage must be done during the bleeding phase of the cycle in order to make the diagnosis.

6. The microscopic picture characteristic of the disease can be reproduced in the endometrium of the normal female by the injection of progesterone during the bleeding phase of the cycle.

7. Administration of progesterone during the latter part of the cycle will delay the onset of menstrual bleeding.

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A STUDY OF THE PHYSIOLOGIC ACTION OF HUMAN CHORIONIC HORMONE*

The Production of Pseudopregnancy in Women by Chorionic Hormone

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IN 1927 the urine of pregnant women was shown to contain a substance which was gonadotrophic in infantile mice. This material was extracted and made available for clinical use a few years later, and is generally known as chorionic gonadotrophin. This material has been extensively studied in the laboratory, and the literature is replete with reports of the effect of chorionic hormone on experimental animals. The results of using this hormone in women are inconclusive and contradictory. Most of the clinical reports deal with cases of an assumed physiologic derangement treated according to a hypothesis developed in the laboratory and transferred to patients. Both the correctness of the diagnosis and the validity of the transfer are often in doubt. Because of this we decided to study the effect of chorionic hormone in *normal* women. This communication presents a series of observations in which large doses of chorionic hormone induced a pseudopregnancy in women (persistence of the corpus luteum, decidual changes in the endometrium, prolonged excretion of pregnanediol, and positive Aschheim-Zondek tests on the urine).

Historical

In a review of the literature up to 1939, Engle¹ concluded that in monkeys and women, treatment with chorionic hormone produced follicular degeneration but the effects on the corpus luteum were equivocal. Hamblen² treated 37 cases of functional bleeding and in no case was there any evidence of induced luteal function. Browne and Venning³ reported that when treatment was started during the luteal phase of the normal cycle there was an increased and prolonged excretion of pregnanediol, and the onset of the next menstrual period was delayed. In 1940 the authors⁴ used doses comparable to those employed by Browne and Venning, but did not observe any alteration in menstrual rhythm or in the cyclic changes in the endometrium during the period of treatment. In some patients there was an amenorrhea of two or three months' duration after cessation of treatment, and the endometrium became atrophic during this interval. In no case was there any evidence of induced or prolonged luteal function. The physiologic action on the corpus luteum of the monkey was investigated by Hisaw.⁵ He found that relatively large doses of pregnancy hormone would prolong the functional phase of the corpus luteum as much as fourteen or fifteen days. Cognizant of the fact that the pregnant woman excretes much larger quantities of chorionic gonadotrophin than does the monkey and of our previous negative findings with doses of 500 R.U. per day, it was decided that the effect of large doses should be determined in normal women. Urinary excretion values of pregnancy indicated that doses of 10,000 to 20,000 I.U. might approximate the amounts normally present in the first week or two of pregnancy.

*Presented as the Prize Award Essay before the Central Association of Obstetricians and Gynecologists, Fourteenth Annual Meeting, Chicago, Ill., Sept. 19 to 21, 1946.

Methods and Materials

Previous clinical experience had shown that larger doses of commercial preparations produced rather severe local reactions in some patients. Furthermore, the contemplated dose could not be given in a reasonable volume if the regular trade preparations were used. Chorionic gonadotrophin (Antuitrin-S) was generously furnished by Parke, Davis, & Company as a dry powder. It was dissolved in a phosphate buffer (pH 7.4) so that each ml. contained 5,000 I.U., and the solution was sterilized by passing through a Jena filter. No preservative was added to these solutions. Check assays on immature rats indicated these solutions were up to expected potency. Women with normal menstrual function were selected for this study, and the effects of treatment were determined by obtaining endometrial biopsies once or twice a week. The urine was collected and processed for pregnanediol by the method of Astwood and Jones.⁶ In several patients scheduled for elective surgery it was possible to observe or obtain an ovary at the time of laparotomy. The injection of these large doses of chorionic hormone did not produce any systemic or local effects of significance. There was never anything more than a mild local reaction which suggests that the preservative used in commercial preparations may be a factor in some of the more extensive local reactions seen previously.

Observations

Two subjects (W. P. and N. W.) received 20,000 I.U. daily beginning in the late secretory phase. The menstrual period was delayed by nineteen days and twelve days, respectively, and during this time decidual changes were present in the endometrium as determined by biopsy (Fig. 1). Bleeding occurred during and despite continued treatment. The subsequent cycles of these patients were normal. The urine of these patients obtained during treatment produced a positive Aschheim-Zondek test.

In the third subject (L. A.) chorionic hormone, 10,000 I.U. daily, was given as indicated, and essentially the same effects were observed. This experiment was terminated by laparotomy on the fourteenth day after starting treatment. Endometrial biopsies had shown a definite decidual reaction, and at laparotomy a well-formed and apparently active corpus luteum was found. This was present twelve days after the expected menses. This corpus luteum was associated with a delayed menstrual period, with a persistence of pregnanediol excretion ten days beyond the usual life span of a corpus luteum spurium, and with a decidual reaction in the endometrium (Figs. 1, and 4 to 7). Urine obtained from this subject on the fourth day of treatment gave a positive Aschheim-Zondek test.

Since doses of 20,000 I.U. and 10,000 I.U. per day had a definite luteotrophic effect and had produced a pseudopregnancy, it was of interest to determine what would be a minimal effective dose. Daily doses of 5,000 I.U. and 2,500 I.U. were tried, and the results are shown in Fig. 1. In the subject (B. L.) who received 5,000 I.U., the duration of the pseudopregnancy was shorter, and the amount of pregnanediol in the urine was smaller. Menstruation started on the thirteenth day of treatment, and at laparotomy the following day the left ovary was removed. It contained a large well-formed corpus luteum and many normal immature follicles. Doses of 2,500 I.U. delayed the onset of menstruation not more than two or three days. In both cases it started after ten days of treatment, and the predecidual changes were no greater than those seen in normal cycles. The quantity of pregnanediol recovered from the urine of one of these patients (M. B.) was larger than from any other patient in this study, and it is peculiar that she started to bleed while the pregnanediol values were still being

maintained. It was not possible to obtain urine for pregnanediol from the other patient receiving this dose. From these observations it appears that at least 5,000 I.U. daily is necessary to produce a definite pseudopregnancy.

It was of interest to study the urinary excretion of chorionic hormone to determine the renal threshold for this substance. After four to five days of treatment the urine was collected and tested by injection of 3 c.c. into immature female rats. The urine of patients receiving 10,000 and 20,000 I.U. daily produced positive Aschheim-Zondek reactions, but the urine of the patients receiving 5,000 and 2,500 I.U. daily was negative. This indicates that the developing trophoblast must produce over 5,000 I.U. daily before the Aschheim-Zondek test becomes positive. Thus it is possible for an early pregnancy to maintain the corpus luteum with an amount of chorionic hormone insufficient to give a positive Aschheim-Zondek test. This may explain the negative Aschheim-Zondek tests in the first few days of pregnancy.

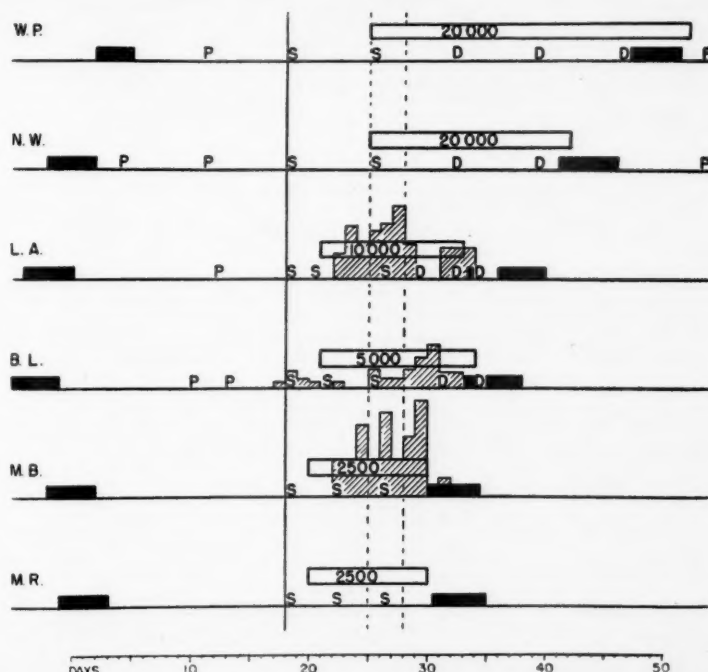


Fig. 1.—Graphic representation of the observations on six subjects in whom treatment was started in the premenstrual (luteal) phase of the cycle. The black bars represent menstruation. The letters represent endometrial biopsies, *P* for proliferative, *S* for secretory, *D* for decidual reaction, and *R* for resting. The vertical line indicates the date of the first secretory biopsy, and the vertical broken lines the approximate interval of expected menstruation. The open bars indicate the duration of treatment, and the numbers denote the dosage of chorionic hormone in I.U. per day. The shaded bars represent the excretion of pregnanediol in mg. per day.

Having demonstrated that chorionic gonadotrophin would prolong the functional life of the corpus luteum, it was of interest to determine whether it would have any effect in the follicular phase of the cycle. Treatment was started in the preovulatory interval in five subjects (Fig. 2), one of them being treated twice (M. J. 1 and M. J. 2). Daily doses of 10,000 I.U. were employed, since this procedure had been found effective when started in the luteal phase of the cycle. In two instances the endometrial biopsies failed to reveal any evidence of a secretory change (I. E. and M. J. 2). In the case of M. J. 2 the interval was short (nineteen days) and the subsequent bleeding was prolonged (thirteen

days). In three cases the cycles were of normal length, and the secretory changes in the endometrium were normal in onset and duration (D. A., M. J. 1, and K. B.). There was no secretory change in the endometrium until after eight days of treatment in two of these patients, so there is no indication that ovulation or the onset of luteal function was hastened. The pregnanediol excretion was of normal duration in L. A., but none was ever recovered from the urine of K. B. except for a trace the day before the onset of bleeding. In only one subject was there a delay in the onset of menstruation and a decidual change which indicated that the therapy had influenced the ovarian cycle (W. P.). These observations indicate that the chorionic hormone may have little or no effect on the maturing ovarian follicle.

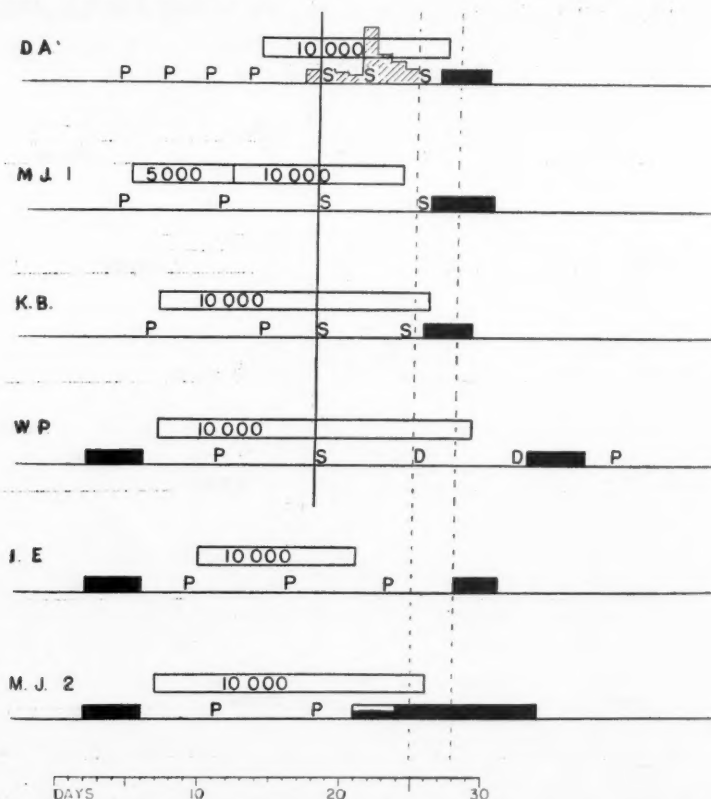


Fig. 2.—Graphic representation of the observations on five subjects in whom treatment was started in the preovulatory (follicular) phase of the cycle. The menstrual periods, biopsies, and treatment are represented in the same manner as in Fig. 1. M. J. 1 and M. J. 2 is the same patient treated at different times.

Two subjects were treated very late in the secretory phase. The initial injection of chorionic gonadotrophin was given within twenty-four hours of the onset of bleeding (N. W. and M. W., Fig. 3). No effect was obtained, so apparently the hormone is unable to revive an involuting corpus luteum.

Chorionic hormone was also given to a castrate (N. D., Fig. 3). This patient had been treated with estrogen and progesterone until the endometrium had developed a secretory pattern. Then injections of chorionic hormone, 10,000 I.U. daily, were given, but had no effect: the endometrium was not converted to a decidua, and the patient menstruated after cessation of the ovarian hormone therapy. This would indicate that the action of the chorionic hormone is through the corpus luteum and not directly on a secretory endometrium.

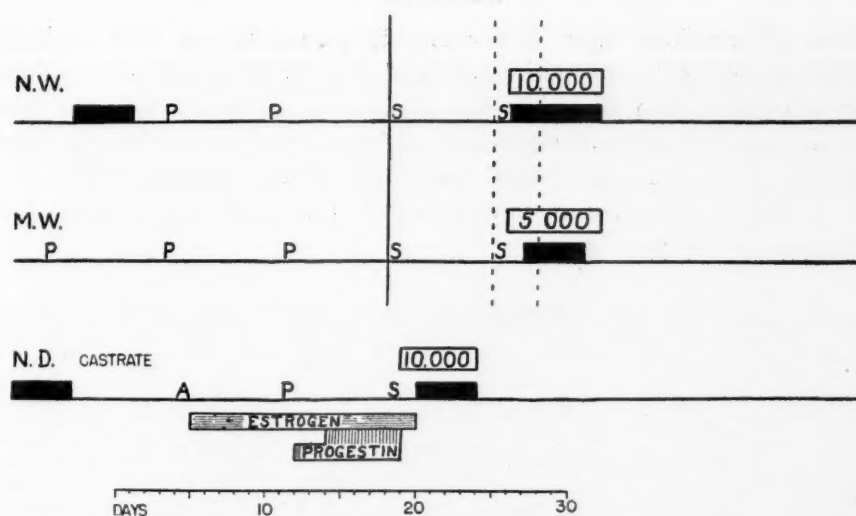


Fig. 3.—Graphic representation of the observations on two patients in whom treatment was started within twenty-four hours of the onset of menstruation and on a castrate patient. The endometrium of N. D. had been developed by administering an aqueous suspension of estrogen (Lakeside) in eight doses of 4 mg. each on alternate days, and progesterone (Lipo-Lutin) in doses of 20 mg. for two days, and then 40 mg. per day for five days.

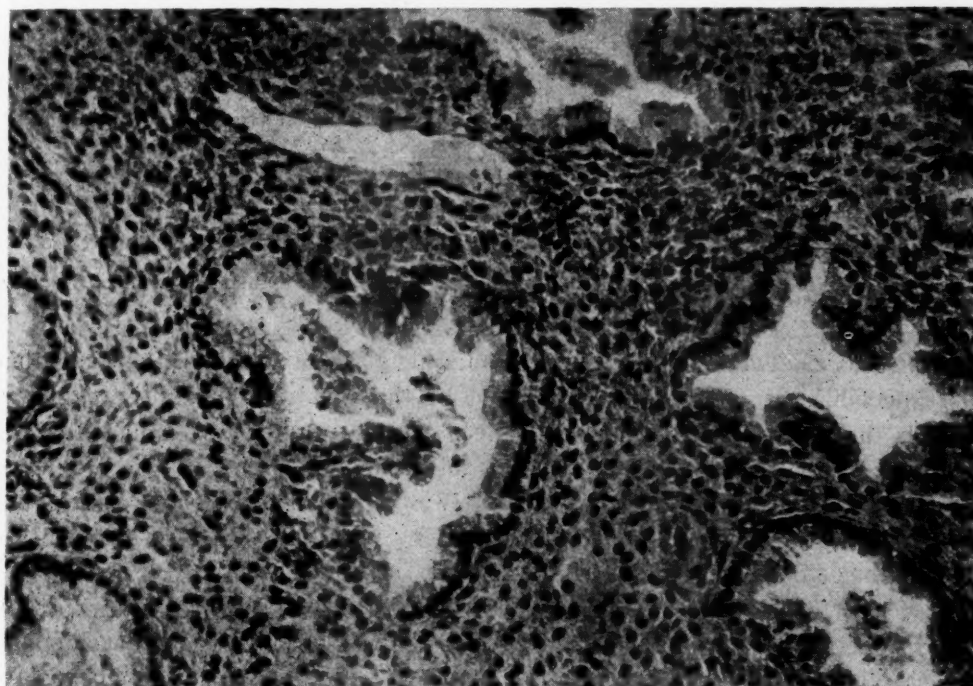


Fig. 4.—L. A. Endometrial biopsy, May 7, on the twenty-sixth day of cycle. Secretory phase. Treatment started the following day.

Discussion

These observations show that chorionic gonadotrophin will prolong the functional activity of a corpus luteum, and thereby give rise to a condition of pseudopregnancy. Also, that chorionic hormone failed to influence the developing follicle, failed to revive a regressing corpus luteum, or to affect the secretory endometrium in a castrate. Since the action of this placental hormone was limited to the maintenance of a pre-existing functional corpus luteum, it appears to be a luteotrophic agent.

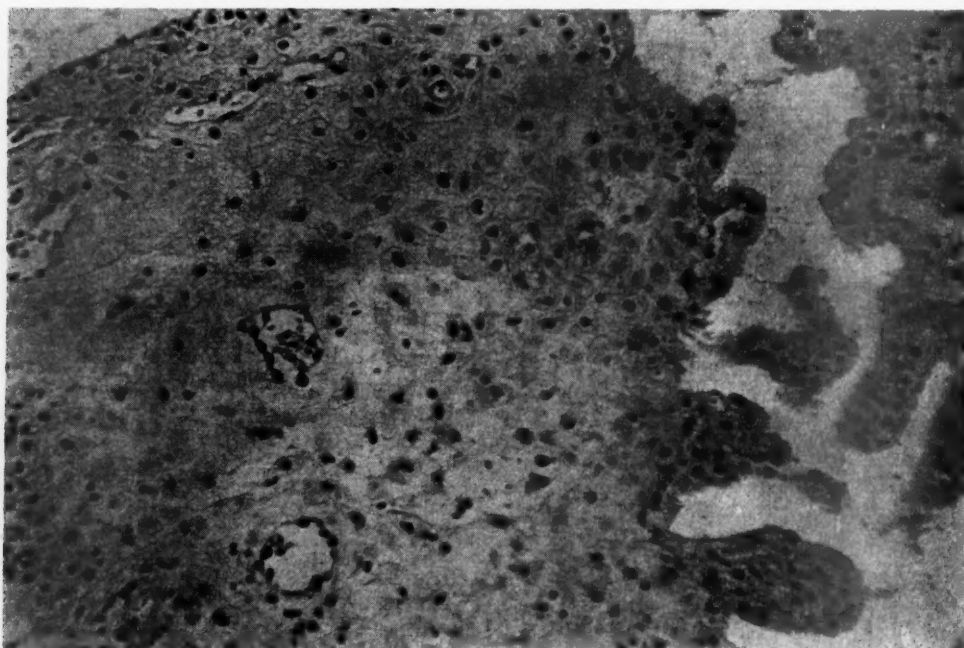


Fig. 5.—L. A. Endometrial biopsy, May 16, on ninth day of treatment, 10,000 I. U. daily. Secretory activity in glands and decidual change in the stroma.

On this evidence it seems that the chorionic gonadotrophin is a hormone that is responsible for the early development of the corpus luteum of pregnancy. This is the first objective study of which we are aware that demonstrates the probable physiologic action of this placental hormone in women. The prolonged excretion of pregnanediol confirms the early report of Browne and Venning, but we cannot confirm their statement that, when treatment is started early in the cycle, it hastens the onset of luteal function.

It is of interest to speculate why human chorionic hormone has not duplicated these results in the experimental animal. In the evolutionary development of the higher forms, some mechanism was necessary to retain the embryo in a place of protection. As one ponders on the transfer from the oviparous to the ovoviviparous to the viviparous mechanisms, it is obvious that some system must be developed which would prolong the time that the embryo would be retained within the maternal system. The literature lists a variety of such mechanisms

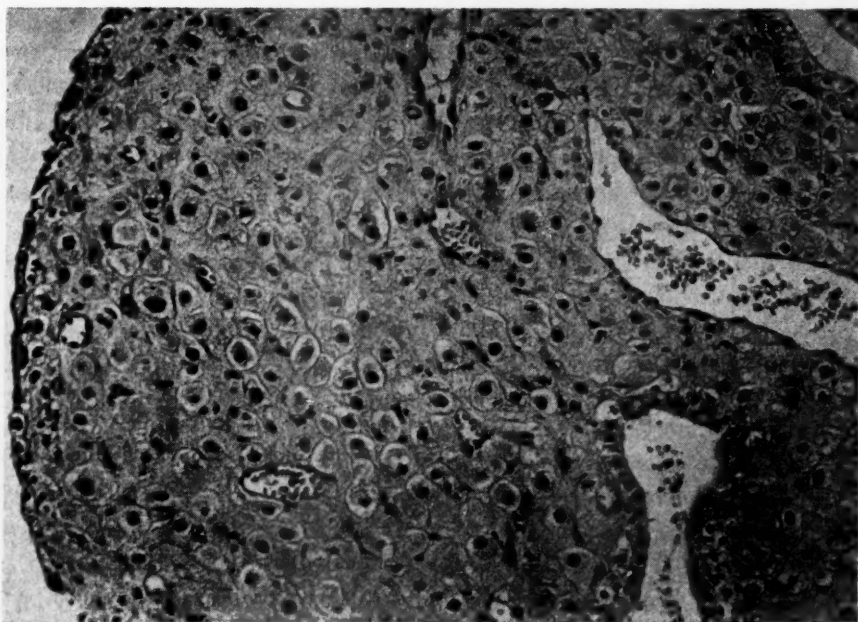


Fig. 6.—L. A. Endometrial biopsy, May 21, on day of laparotomy. Fourteenth day after starting treatment. Menstrual period delayed twelve days. Marked decidual change and increased vascularity.

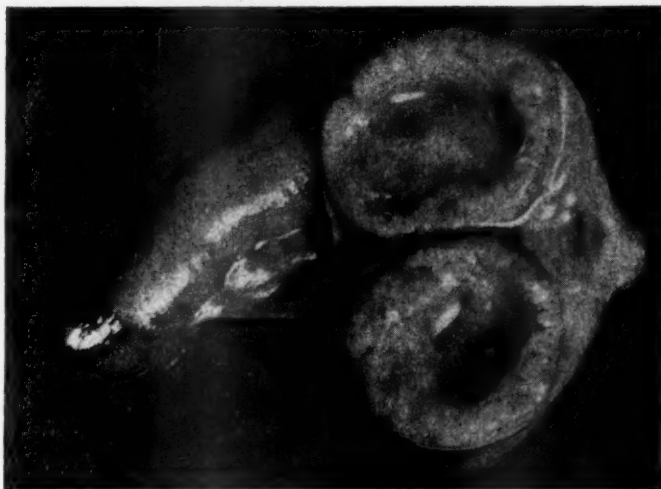


Fig. 7.—L. A. Ovary and tube removed May 21. Ovary cut open to show the large cystic corpus luteum. Treatment started fourteen days previously, menstrual period delayed twelve days.

developed by the different species. The mammalian group has developed the highly specialized placenta which takes over an endocrine function. The placental tissue in mares, monkeys, and women produces a substance which gives an Aschheim-Zondek reaction. The placenta of most other species does not produce this type of gonadotrophic agent. However, the rat placenta has been shown to contain a substance capable of prolonging the function of the corpus luteum in the adult rat.⁷ This luteotrophic extract was also effective in maintaining the corpus luteum after hypophysectomy, but it was devoid of any follicle-stimulating or luteinizing action in the infantile rat.

The hormone of pregnant mare's serum is peculiar in that it is not excreted in the urine, and, when tested in the infantile rat, it produces extensive follicular stimulation. Human placental hormone is excreted in the urine and it produces marked luteinization of the infantile rat ovary. The chorionic hormone of human pregnancy urine should be recognized as a primate pregnancy hormone since it does not exist in any of the subprimate animals. Thus, it appears that horse chorionic hormone in the horse, rat chorionic hormone in the rat, and human chorionic hormone in the human all have a similar luteotrophic effect which may be species specific, but, when these placental substances are injected into foreign species, they may not exhibit a typical luteotrophic action.

The chorionic hormone, being a pregnancy hormone, would logically be used as replacement therapy in abnormalities of early pregnancy. On this basis, it might be indicated in preventing abortion in patients if the threatened or habitual abortion was due to a failure of the trophoblast to produce adequate amounts of luteotrophin. It might also be indicated in certain sterility problems where luteal function may be inadequate for implantation. Aside from pregnancy, it might be of benefit in certain types of menorrhagia due to defective luteal function. Since the luteotrophic action of the chorionic hormone is the only objectively demonstrable action in women, it would not be indicated for the treatment of amenorrhea or anovulatory sterility.

While the doses of chorionic hormone used in this study seem large in terms of previous clinical practice, it should be recalled that the normal amount of chorionic hormone in the urine of early pregnancy often exceeds 200,000 I.U. per day. Common clinical dosage has been based on commercial costs and tolerated doses rather than physiologic requirements.

Summary

1. Human chorionic hormone is luteotrophic in women and will induce a pseudopregnant condition, as evidenced by a prolongation of the functional life of the corpus luteum, the development of a decidua, and the prolonged excretion of pregnanediol.
2. The effective dose of chorionic hormone seems to be 5,000 I.U. to 10,000 I.U. daily. These doses may be given without untoward reactions.
3. Until objective evidence of other gonadotrophic action in women is obtained, the use of human chorionic hormone should be directed toward the maintenance or augmentation of luteal function.

The authors express their appreciation to Doctor J. R. Porter of the Department of Bacteriology for his assistance and cooperation in the preparation of the Jena filters.

Through the courtesy and cooperation of Doctor A. Soucek patients at the Mount Pleasant State Hospital were made available for these observations.

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COMBINED EVIPAL AND SCOPOLAMINE ANALGESIA AND CYCLOPROPANE ANESTHESIA IN OBSTETRICS*

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THE demand of the obstetric patient for the relief of pain during labor has become almost universal. The desire for alleviation of pain during parturition is as old as the beginning of the human race. Much progress has been afforded the patient during the last thirty-five years. But in her intense desire to avoid pain the patient picks up from lay press, motion pictures, and radio many misconceptions. It seems a pity that medical research is not more careful in reporting tentative findings, and that lay sources are not more responsible in interpreting these articles to the public.

I am certain we all agree that anesthesia can usually be produced by introducing an anesthetic agent into either the caudal or spinal canal. However, physicians know that before these methods can safely be publicized to the laity there must necessarily be a great deal of laborious observation recorded on a large series of patients. Such careful testing should certainly precede enthusiastic claims for any anesthetic before it is publicized to the laity. We must bear in mind that no anesthetic agent, whether it be given by inhalation or injection either intravenously, rectally, or by means of the caudal or spinal canal, can be administered without increasing to some degree the percentage of maternal and fetal mortality. It is the duty of the research worker through meticulous animal and clinical experimentation scrupulously to weigh his findings before passing them on to the clinician. If this careful scientific approach is used in studying the actions of analgesics and anesthetics, the obstetric patient will be guided by her physician, who will utilize the safest method appropriate to her individual case; and she will not demand some particular method of pain alleviation suggested by an ill-informed lay person.

In 1941, with Bohlender,¹ the writer described the amnesic action of evipal soluble given rectally and scopolamine hydrobromide given hypodermically in a series of 53 cases studied at the University Hospital. Actual anesthesia at time of delivery was accomplished by the inhalation of ether. Our conclusions stated that evipal soluble given rectally was a safe and effective analgesic; that its amnesic effect was greatly enhanced by the use of scopolamine hydrobromide given hypodermically; and that this method of analgesia was sufficiently satisfactory to merit further study in a larger series of cases. Since the publication of this paper, very few articles describing the use of these drugs in obstetrics have appeared in the literature. Thoms and Taylor² reported favorably upon their use in 110 unselected obstetric patients. They substantiated our conclusions and stated their belief that evipal soluble and scopolamine given

*Presented before the Central Association of Obstetrics and Gynecology, Fourteenth Annual Meeting, Chicago, Ill., Sept. 19 to 21, 1946.

in proper sequence and with suitable selection had satisfactory and safe results. The ease of administration and effectiveness of amnesia of these drugs have been proved by various other workers, as Gwathmey,³ Siegler and Beris,⁴ McNellis,⁵ and E. Petersen.⁶

In order to present a larger series of cases, 700 private obstetric cases at the Immanuel Hospital were studied, wherein evipal soluble was used rectally and scopolamine hydrobromide hypodermically, combined with cyclopropane anesthesia. These cases were delivered during the interval of January, 1941, to June, 1946. The major portion of this time represents the recent war period when the ranks of the nursing and intern staffs were sorely depleted by mobilization of medical personnel into the Armed Forces. The Immanuel Hospital is a general hospital of 175 beds, with the obstetric department housed on one floor segregated from the rest of the hospital. The average number of cases delivered by all physicians per year was 850. These were cared for by the attending staff, the majority of whom were certified obstetricians. No resident physician was in attendance; the intern staff was augmented by senior medical students. Thus, it is plain to see that if analgesia was to be used, it must have a wide margin of safety and be easily administered by nurses who could sit with patients throughout their labor. The cyclopropane was administered by qualified registered nurse anesthetists.

Administration and Dosage of Evipal Soluble and Scopolamine Hydrobromide

A change in dosage of evipal soluble from that of the first series of cases was found to be effective. Whereas the average dosage of evipal at first was 1 Gm., in this study the dosage was increased to an average of $1\frac{1}{2}$ Gm. given rectally. The technique of administration remained simple. All patients upon being admitted to the obstetric pavilion were given a cleansing enema. Thus it was not necessary to repeat this procedure before administration of the drug.

The criteria used in determining the proper time for the administration of analgesia were: (1) when it was definitely ascertained that the patient was in true labor; (2) when she began to complain of pain and ask for relief; and (3) after the cervix showed effacement and three or more centimeters of dilation. Evipal soluble crystals ($1\frac{1}{2}$ Gm.) were dissolved in 60 c.c. of tap water. The patient was instructed to lie on her left side, and an ordinary soft rubber catheter was inserted, usually 4 to 5 inches into the rectum so that the tip of the catheter would remain above the level of the presenting part of the fetus, so the flow of the solution would not be inhibited. The evipal mixture was allowed to flow through a funnel into the catheter by gravity. The buttocks were pressed together for about ten minutes, especially during the time the patient was experiencing pain. A digital rectal examination was not done for at least thirty minutes after withdrawal of the catheter.

Scopolamine hydrobromide ($\frac{1}{150}$ grain) was given hypodermically at about the same time as the rectal instillation of evipal. An additional hypodermic injection of scopolamine hydrobromide ($\frac{1}{200}$ grain) was given one hour after the first injection or later during labor, if considered necessary for good amnesia. In only 25 per cent of cases was this considered necessary. In only one case in this series was it necessary to repeat the administration of evipal. Cyclopropane gas, given by inhalation for anesthesia, was not employed until the presenting

part caused perineal signs denoting imminent delivery, and then only after the patient had been transported from the labor to the delivery room.

Effect of Drugs Upon the Mother

The analgesic and amnesic effect of the combination of evipal and scopolamine was most gratifying.

The rapidity of action is one of the most startling qualities of evipal given rectally. Some patients became drowsy and sleepy within three minutes; others, not before ten minutes; the average time was five minutes before the patient was asleep. Ordinarily the patient slept soundly between uterine contractions, but was aroused while having a pain, only to lapse into unconsciousness after its completion. After labor has actually begun and the cervix effaced and dilated sufficiently, the drugs may be given with benefit any time during the course of labor, but the earlier they are given, especially in multiparas, the more complete the sedation.

It is necessary for a nurse to be in constant attendance upon the patient while in labor. Only 5 per cent of patients were difficult to manage while having pain. These thrashed about the bed, wanted to sit up, get out of bed, et cetera. All of these patients were unaware of their actions, and reported total amnesia regarding their labor.

Complete analgesia and amnesia during labor were experienced by 93 per cent of the patients studied. Upon being questioned, they all volunteered that they remembered nothing about their labor after rectal instillation of evipal. The average patient slept from one and one-half to two hours after her delivery. Upon waking, the majority of mothers inquired when they might expect the birth of their baby. Seven per cent of the patients received only fair sedation, and some remembered almost everything about their labor until the time of administration of cyclopropane, while others had a hazy recollection of pain and discomfort up to the time of anesthesia. A review of their charts showed that the majority of these patients had been given castor oil for induction of labor. Since then, castor oil has been eliminated in the routine of induction of labor, and no failure to produce good amnesia has been encountered.

No maternal deaths were reported.

The length of labor was not increased, and textbook figures for the duration of labor were actually shortened, since the drugs do not diminish either the intensity or duration of the uterine contractions once the patient is in actual labor. However, if sedation is given too early, i.e., before pains are well established and before effacement and dilatation of the cervix have begun, the patient may go to sleep and labor pains stop entirely. In primiparas, the average length of labor was eleven hours and thirty-nine minutes; in the multiparas, nine hours and forty-one minutes.

Although evipal is reported to be detoxified rapidly in the liver⁷ there is no clinical evidence to cause hesitation in using this drug in pre-eclampsia. Twenty cases of mild and severe pre-eclampsia were encountered in this series in which evipal and scopolamine were used as sedation. One primipara who became mildly toxic during her last week of pregnancy delivered normally, but developed postpartum convulsions within two hours following delivery. Recovery was prompt after dehydration therapy was instituted.

Administration of Cyclopropane

Cyclopropane gas (C_3H_6) was first used as an anesthetic in surgery by Waters⁸ in 1934. A colorless, nonirritating gas with a sweet odor and taste, it has the most powerful anesthetic potency of any of the gaseous anesthetics,

according to Lull and Hingson.⁹ It is highly inflammable. In 3 to 5 per cent concentration it will produce analgesia; 6 to 8 per cent will produce unconsciousness; 20 to 25 per cent will maintain surgical anesthesia. This gas has two very important properties which are highly acceptable for obstetric deliveries, e.g., rapidity of action, and no effect of decreased uterine contractions during light anesthesia. The high percentage of oxygen used in combination with cyclopropane is also highly favorable to both mother and child.

As previously stated, cyclopropane is not administered until the patient has been transported to the delivery room and birth of the child is imminent. The actual administration of cyclopropane is entrusted to one of three qualified nurse anesthetists, who are alternately on call for obstetric anesthesia. The gas is given through a closed system machine. The face piece is secured over the nose and mouth, and the patient is given a few inhalations of 100 per cent oxygen before this concentration is diluted with 50 per cent cyclopropane. As unconsciousness ensues, the mixture may be reduced to 10 to 15 per cent cyclopropane and 85 per cent oxygen. The depth of anesthesia is markedly increased during labor pains. With effective evipal-scopolamine analgesia the mixture of cyclopropane may be reduced to as little as 3 to 5 per cent. The proportion of cyclopropane-oxygen is maintained until after the birth of the baby, whereupon the oxygen content is again raised until the umbilical cord is severed. If repair of an episiotomy or laceration is necessary, the concentration of cyclopropane may be raised to 15 to 20 per cent, to maintain surgical anesthesia.

Because cyclopropane is highly inflammable and explosive, certain precautions must be insisted upon in its administration. Every precaution against the production of static sparks was used. In the delivery room all electric lights were turned on before the gas was used; no rubber-soled shoes were worn; and no smoking was allowed near the delivery rooms. Cyclopropane was curtailed during electric storms. The patient and anesthetist were meticulously grounded to prevent disaster. As a further safety measure, helium has been introduced to act as a buffer against explosion by reducing the oxygen ratio. Thomas¹⁰ has suggested the employment of inert helium in the initial flow of anesthesia to the patient; he recommends 1,000 c.c. of helium, 500 c.c. of cyclopropane, and 500 c.c. of oxygen. After three minutes the helium is reduced to a flow of 150 c.c. Oxygen is carried at the metabolic need of the patient, usually from 300 to 500 c.c. and cyclopropane allowed to flow at the rate of 50 to 200 c.c. according to the requirement for anesthesia. In our series of cases, no explosions were encountered.

Effect Upon the Baby

In this statistical study all cases which required elective cesarean section from whatever cause were excluded. The total number of babies delivered was 705, including five sets of twins; 674 presented by the vertex and of these 602 were occiput anterior; 50 were persistent occiput posterior; 22 were transverse arrests. The number of breeches was 31: complete breeches, 24; single or double footling, 7. The number of stillbirths was 4, the causes of which were found to be the following:

1. Full-term infant born with a meningocele.
2. Seven-month gestation complicated by placenta previa marginalis.
3. Missed labor—near full term—no fetal heart or movements three weeks prior to delivery.
4. Double footling; membranes ruptured at home and nonpulsating umbilical cord presenting at the vulva upon hospital admission.

This list shows clearly that the analgesia and anesthesia given during labor in no way caused the small number of stillbirths reported.

No actual fetal asphyxia was encountered. The majority of all babies cried spontaneously a few moments after being born. Fifty babies required resuscitation. The majority of these cried shortly after delivery, but did not breathe well subsequently. After the usual procedure of clearing the air passage of mucous and placing the baby in a respirator for a few moments, all regained normal respiratory function directly and gave no further concern. Although barbiturates are known to pass through the placenta to the fetal circulation, there seemed to be no evidence of harm to the fetus when evipal was given late in labor. Several patients did not receive their sedation until within one hour of delivery; one multipara only thirty-two minutes before delivery.

Cervical Laceration

As a customary routine procedure following the third stage of labor, the cervix of each patient was examined carefully for possible laceration. When lacerations were found with frank bleeding or enough extensiveness to delay postpartum healing, all such tears were immediately sutured and this fact recorded on the patient's labor record. The total number of such lacerations in this series was 31. One secundogravida, after a long hard labor with complete effacement of the cervix and with no dilatation greater than 3 cm., required Dührssen's incision of the cervix to facilitate delivery.

Instrumental Deliveries

Table I represents a summary of instrumental aids used in delivery of 705 babies.

TABLE I

1. Low (perineal) forceps—312—44%
a. Primiparas—212
b. Multiparas—100
2. Midpelvic application—47—6%
a. Primiparas—22
Kielland rotation for occiput posterior—10
Kielland rotation for occiput transverse—12
b. Multiparas—25
Kielland rotation for occiput posterior—11
Kielland rotation for occiput transverse—11
Tucker-McLean rotation for occiput transverse—3
3. Breech delivery—31
Piper forceps for aftercoming head—5

In the primigravida there was no hesitation in applying forceps to the head of the child prophylactically when the presenting part was on the perineum. This was generally done after performing an episiotomy, a maneuver necessary in less than half the number of multiparas. The use of perineal forceps definitely shortens labor and also acts as a protective measure by diminishing trauma to the fetal skull. There is no evidence of increase in the incidence of midforceps application in this series.

Discussion

The purpose of this report is to present a statistical study of the amnesic action of a little publicized barbiturate combined with scopolamine in a large enough series so that certain clinical conclusions may be drawn. Inasmuch as cyclopropane has proved to be an effective anesthetic when used with sedatives

other than evipal, we were curious to study the combined actions of evipal, scopolamine, and cyclopropane.

The ideal, safe, flawless anesthetic has not yet been discovered. Any form of anesthesia or analgesia has its drawbacks. In obstetrics we must consider the effect of the drug upon both the mother as well as the child in utero; also the ease with which the drug is administered. These are the deciding factors as to the practicability of any form of obstetric analgesia.

The patients studied in this series represent a cross section of middle class private obstetric clientele in a midwestern locality. The heritage of most of these patients was north European stock; very few were of Latin extraction. All patients were given many months of careful prenatal care, and were told they could expect a certain amount of pain and discomfort during the early portion of their labor. They were promised no particular kind or type of anesthesia, but were assured that all possible relief would be afforded them when labor had reached the point at which sedation would not inhibit further progress, and would not be harmful to either the patient or unborn child. This method of psychologic preparation for labor thus prepared the patient to expect some discomfort in early labor; no patient was promised that labor would actually be painless. The production of a proper mental attitude by allaying fear has much to do with increasing the sedative value of any drug employed.

This combination of analgesic medication is useful in any hospital obstetric department which is sufficiently staffed to carry out the simple technique outlined in this report. It seems particularly applicable to the maternity pavilion in a general hospital where the attending physician must rely upon competent interns and nursing staff to carry out sedation under his direction, but without his constant attendance throughout the labor. Anesthesia induced by cyclopropane cannot be entrusted to a novice but only to a well-trained and qualified anesthetist. Such a person should be a full-time hospital employee and need only be in attendance for the actual delivery of the baby.

During the time these 705 cases were being studied, various combinations of other anesthetics were tried, i.e., 1 per cent novocain by pudendal block, nitrous oxide, and ether. With the latter two the uterine action was slowed prior to delivery, and greater delay in fetal respiratory action seemed evident. Several times when an anesthetist was not available, pudendal block by using 1 per cent novocain worked admirably. Its striking attribute was the ease with which the perineal floor relaxed, allowing the presenting part to be born often without a laceration or the necessity of an episiotomy. The ease and apparent safety of administration was also striking.

Irving¹¹ states that the combination of barbiturates and scopolamine would be ideal if it were not for the fact that they produce unfavorable maternal and fetal respiratory complications. No maternal respiratory complications of any variety were encountered in this series while using evipal and scopolamine. Less than 7 per cent of the babies required resuscitation. Of these, all breathed normally following artificial resuscitation and gave no further trouble. This small percentage may be attributed in part to the high ratio of oxygen carried while using cyclopropane.

Five per cent of our patients became difficult to manage under evipal and scopolamine. This is a strikingly smaller proportion than is reported with use of other barbiturates and scopolamine.

The number of instrumental deliveries will be increased whenever sedation is employed. Inhalation anesthesia usually increases the necessity for the application of forceps; especially true in the use of ether, due to the abolition of uterine contractions. Cyclopropane has the advantage of not decreasing uterine contractions materially; thus it reduces the use of forceps to the outlet variety when the head is actually on the perineum. There is no contraindication in using evipal-scopolamine combination in multiple pregnancies, forceps rotation of occiput posterior and transverse arrests, or in breech deliveries.

Cyclopropane should not be used in doing internal podalic versions. The uterine muscle cannot be relaxed sufficiently to permit accomplishing this obstetric operation safely.

On three occasions the progress of labor was inhibited due to the existence of Bandl's contraction ring. Adrenalin was given, and the anesthetic was changed from cyclopropane to ether. No untoward reaction was noted in using adrenalin while cyclopropane was being administered.

No evidence of cardiac irregularities was seen in any patient studied in this series.

Blood loss was not actually measured in this series, but the average loss per case could be estimated at less than 400 c.c., thus substantiating Greenhill's¹² observation with regard to cyclopropane. Due to the high concentration of oxygen in the anesthetic mixture the blood appears much redder than when nitrous oxide, for instance, is used, thereby giving the impression of greater blood loss.

No evidence of proctitis following rectal instillation of evipal was observed in any case in this series.

Effective sedation is considered an aid in cervical dilation, since it reduces spasticity of the cervical muscle fibers and thereby minimizes the incidence of cervical laceration. Inspection of each case in this series for cervical laceration showed a total number of 4 per cent. Because the cervix is not generally inspected following the third stage of labor, statistics concerning cervical laceration are not dependable.

Conclusions

1. After carefully evaluating clinical data on 700 private obstetric cases, the combined amnesic and anesthetic action of evipal soluble given rectally, scopolamine hydrobromide given hypodermically, and cyclopropane administered by inhalation was found to be safe and effective.

2. Analgesia and amnesia were produced completely in 93 per cent of cases; 7 per cent experienced little or no relief of pain.

3. Four stillbirths were reported. The cause of each was ascertained, and in no instance did the agents used for the production of analgesia and anesthesia have the remotest connection with etiology of the fetal death. Less than 7 per cent of newborn babies required artificial resuscitation. All of these survived with no further trouble after resuscitation.

4. The technique of administration of evipal and scopolamine is simple, and the action is especially rapid. The use of these drugs does not increase the need for additional nursing care over any other form of analgesia.

5. Cyclopropane is especially adapted for obstetrics because its anesthetic action is rapid and because its high oxygen content lessens fetal and maternal respiratory complications. It is highly inflammable and should be administered by a trained anesthetist only after all precautions have been taken to prevent explosions.

6. About 5 per cent of patients became difficult to manage while under sedation. This is an improvement over results with most barbiturate-scopolamine combinations.

7. Cervical lacerations in all cases amounted to 4 per cent, and were repaired immediately following delivery, whether actually bleeding or not. This small incidence of laceration speaks well for the relaxing effect of evipal and scopolamine upon the cervical muscle fibers.

8. There is an increase in the proportion of perineal application of forceps in vertex presentation, especially in primigravida, whenever analgesia and surgical anesthesia are used.

I wish to express my appreciation to Dr. Burnell V. Reaney for help in gathering statistics for this paper; to Doloris Broughten, R.N., Ruth Omig, R.N., and Mabel Owen, R.N., for their efficient administration of the cyclopropane used in these studies, and also for their help in preparing the data for the paragraph on the use of cyclopropane.

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SURGICAL GERIATRIC GYNECOLOGY*

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THE progressive trend toward the prolongation of the life span in the United States has made gynecologists aware of the increasing demand for the care of these elderly women. Hippocrates emphasized the need for special study and observation of senile changes and, in the eighteenth and nineteenth centuries, Floyer, Constatt, Seidel, Charcot, and others directed attention to the medical care of the aged.¹ In recent times Boas,² Thewlis,³ and Kosmak⁴ have stimulated interest in the patient past 50 years of age. Thus, the development of geriatrics has been slow, but surgical treatment of the aged has been particularly slow, as indicated by the few reports of studies of any large series of cases. Therefore, the following study merits attention, since it reviews the results of previous studies of gynecologic surgery in the aged, analyzes a statistical study of a fairly large series of patients, and attempts to further evaluate the advantages and conditions for gynecologic surgery in the aged, and possibly established operative mortality rates for these age groups in relation to life expectancy.

At the time of the American Revolution the mean length of life was 35.5 years; by 1900 it had risen to 50 years, and today it is over 64 years. The average expectation of life at birth for white females in the United States is 68.6 years.⁵ Application of the present knowledge of medicine and hygiene should make it possible to extend the average length of life to about 75 years. Future medical discoveries may extend this by many years.

Nichols⁶ attempts to present life expectancy according to mathematical deductions and states that nothing is more uncertain than one life; nothing is more sure than the law of averages on a million lives. The expectancy tables of the insurance companies furnish an absolute yardstick to measure, not one life, but the average of a group. At the age of 50 and in good health, one has an expectancy of 20 years. For each year one lives in good health beyond 50, one-half year is added to seventy. Thus, at 60, one could reasonably expect to reach 75; at 80, to just fall short of 85. Therefore, the life expectancy may be weighed against the mortality rate of the operation. At present, the mortality rates of gynecologic surgery in the aged woman have not been established.

In considering the aged woman (arbitrary basis, 60 years), much good may be achieved in prevention by periodic examination and by instituting proper therapy at an earlier and more desirable age when there is a greater resiliency of the body, organs, and tissues. But there are still the multitudes of old women who come for relief of a large number of gynecologic conditions rather late.

*Presented before the Central Association of Obstetricians and Gynecologists, Fourteenth Annual Meeting, Chicago, Ill., Sept. 19 to 21, 1946.

For a long time these women have been considered beyond the time for any surgery and have been dealt with only palliatively and not satisfactorily. That this attitude is wrong and that these older women can tolerate surgery is supported by the following reports. Goldsmith⁵ reported on the surgical care of ovarian tumors, 88 past 50 years, and 10 past 65 years, in a series of 344. Although this age group of patients are frequently more prone to have medical complications (cardiovascular, pulmonary, or renal) yet these complications were not sufficient to contraindicate surgery.

Kosmak⁴ published his results from a questionnaire study in 1942. From Johns Hopkins Hospital, Te Linde sent the following statistics: 167, or 4.1 per cent, out of a total of 4,071 (from Jan. 1, 1940, to Jan. 1, 1942) were 60 years or over. In 112 operations of all types, 41 were well, 61 were improved, 7 unimproved, 3 died (due to coronary occlusion, pyelonephritis, and one was moribund from carcinoma of the bladder). He prefers pentothal sodium as an anesthetic. From Mayo Clinic, Mussey reported on statistics from 1939 to 1941; among 27,140 patients, gynecologic patients over 60 years numbered 2,430, including 390 breast cases; 585 operations were performed with three deaths, including one each from pulmonary embolism, glomerulonephritis with uremia, and pneumonia. There were 413 patients operated upon for rectocele, cystocele, and prolapse with over 95 per cent either completely cured or improved. The five-year survival rate for malignancies of the pelvic organs was 55 per cent. General anesthesia was usually employed, with spinal anesthesia, in a fair proportion of suitable cases. Maxwell reported from the University of California Hospital, 69 patients over 60 years in a series of 680 gynecologic patients in 1939 with no operative deaths, although many had hypertension and two were diabetics. The Bellevue Hospital report by Studdiford presented 7,971 gynecologic patients in a recent year; 154 were over 60 years of age. There were 63 operations, of which 28 were majors; there were 19 deaths in the entire series, of which 10 were claimed to be nonoperative. W. C. Danforth had 63 operations in patients between 60 and 75 years including breast cancers. He had no operative deaths. Ethylene was used in all but one patient. Kosmak felt that there need be no hesitancy in attacking gynecologic problems in older women because of the understanding of underlying factors and the developments in pre-and postoperative care and improved anesthetic procedures.

Liccione⁶ obtained good results in 9 patients 63 to 96 years of age, with complete procidentia treated by the LeFort operations.

Newton⁷ had eight operative deaths in 98 major surgical operations in patients over 70 years of age. In addition to the above, there were single case reports of operations in women of 80 and 102 years of age (de Filippi,⁸ Ladwig,⁹ Horta Barbosa,¹⁰ Christitch,¹¹ Morton,¹² and Clark.¹³

Material

The case records of 313 women, 60 to 87 years of age, were studied. (See Tables.) These patients were on the gynecologic services of Cook County (196), Michael Reese (76), and Mt. Sinai Hospitals (41).

TABLE I. AGE INCIDENCE (60-87 YEARS)

AGE 60-65	66-70	71-75	76-80	81-87
173	89	29	18	4
55.3%	28.4%	9.3%	5.8%	1.2%

TABLE II. INCIDENCE OF SIGNIFICANT MEDICAL CONDITIONS

HYPERTENSION	DIABETES	HEMIPLEGIA	ASTHMA	ARTHRITIS	PSYCHOSIS
217 (over 140 systolic) (272 recorded)	12	7	5	4	1
80%	3.8%	2.2%	1.6%	1.3%	0.3%
111 (over 170 systolic) 40.5%					

Table II, which is a record of significant medical conditions, is probably incomplete, but the incidence of hypertension (80 per cent over 140, 40.5 per cent over 170) is common and is only of importance if associated with renal or myocardial damage. Wosika and Maher¹⁴ found hypertension in 76 per cent of 97 cases of prolapse of the uterus. They suggested that prolapse of the uterus with resultant ureteral obstruction and hydronephrosis causes a decrease in the renal blood supply and hypertension. The other medical conditions in this age group require study and proper evaluation as to the patient's capabilities to tolerate anesthesia and operative procedures; this medical determination may require medical consultation.

TABLE III. CLINICAL PELVIC FINDINGS

<i>Pelvic Herniosus</i>	
Procidentia uteri with cystocele and rectocele	114
Prolapsus uteri with relaxed pelvic floor	52
Prolapsing cervical stump with cystorectocele	8
Cystorectocele	44
Urethrocyctocele	12
Ulcerated neoplasms of labia	5
Carcinoma of vulva	1
Carcinoma of right bartholin gland	1
Infiltrating carcinoma of urethra	1
Prolapsus urethrae	1
Vaginal bleeding	3
Vesicovaginal fistula	1
Neoplasm of corpus uteri (large or nodular corpus)	29
Abdominal mass	46
Ovarian cyst (by peritoneoscopy) (1 had been tapped five times a year for ascites for a year and one-half)	5
Ventral hernia	2
Cyst of vulva	1

It is of interest to note the predominance of pelvic herniosus (230) in the clinical pelvic findings (Table III). For many years this condition has been considered innocuous, and treatment was carried out only to relieve the discomfort of the patient. In addition to relieving the patient of her incapacitating condition, it is also important to keep in mind the effect of the prolapsed uterus and the pelvic hernia on the ureters and kidneys, as demonstrated by Wosika and Maher.¹⁴ The remaining clinical conditions demanded treatment for the patient because of malignancy of the lesions. Occasionally, an unsuspected carcinoma of the corpus uteri was found in a prolapsed uterus, as well as other pathology such as fibroids, polyps, and adenomyosis.

Table IV on pathology reveals the high incidence of malignancy of the generative tract in this age group as well as benign neoplasms. Leucoplakia of the cervix is a lesion requiring eradication because of its neoplastic tendencies.

The operative procedures in Table V show the trend toward vaginal hysterectomy and pelvic herniorrhaphy (anterior colporrhaphy and perineorrhaphy) for pelvic herniosus in old women, rather than the Watkins' interposition, LeFort, or Manchester plastic. In view of the high incidence of neoplasms

TABLE IV. PATHOLOGY IN THE 313 ELDERLY WOMEN

Adenocarcinoma of corpus	24
Squamous cell carcinoma of corpus	2
Fibroids of corpus	43
Fibrosis and adenomyosis	34
Endometrial polyps	9
Squamous cell carcinoma of cervix	1
Leukoplakia of cervix	21
Acanthosis and ulceration of cervix	1
Chronic cervicitis with polyps	33
Tuberculosis of cervix	1
Papillary adenocarcinoma of ovary	16
Multilocular serous cystadenoma of ovary	11
Multilocular pseudomucinous cystadenoma of ovary	5
Multilocular bilateral Brenner tumors of ovaries	1
Fibroma of ovary with cystic degeneration	2
Cystic teratoma of ovary	1
Squamous cell carcinoma of vulva	6
Adenocarcinoma of Bartholin gland	1
Transitional cell carcinoma of urethra	1
Urethral caruncle	1
Pelvic abscess	1
Hematoma of rectus muscle	1
Adenocarcinoma of large bowel (one primary, one secondary)	2

TABLE V. OPERATIONS

Vaginal hysterectomy, anterior and posterior plastic	110
Vaginal hysterectomy, bilateral salpingo-oophorectomy	7
Vaginal hysterectomy and posterior plastic	28
Vaginal hysterectomy and colpocleisis	3
Watkins' interposition and posterior plastic	7
Vaginal defundation	1
LeFort and posterior plastic	24
Manchester plastic and posterior plastic	4
Cervicectomy, anterior and posterior plastic	10
Cervicectomy and colectomy	1
Total colpocleisis and posterior plastic	2
Anterior and posterior plastic	38
Partial resection of urethra	1
Abdominal hysterectomy	1
Subtotal hysterectomy	3
Subtotal hysterectomy and bilateral salpingo-oophorectomy (Two with appendix)	18
Abdominal total hysterectomy, bilateral salpingo-oophorectomy	21
Abdominal fixation of corpus uteri	1
Abdominal fixation of vaginal vault	1
Exploratory laparotomy	8
Dilatation and curettage, bilateral salpingo-oophorectomy	1
Unilateral oophorectomy	17
Bilateral oophorectomy	2
Vulvectomy (3 with Bassett operation) (Stoeckel)	8
Ventral herniorrhaphy	1
Closure of colostomy and left oophorectomy	1
Incision and drainage of rectus hematoma	1
Resection of colon and first stage Mikulicz	1

in this age group, vaginal hysterectomy further seems the most desirable operative procedure for the prolapsing uterus. The variety of gynecologic operations indicates the feasibility of performing any type of gynecologic surgery in this age group.

The choice of anesthetic is indicated by the high incidence of local anesthesia (1 per cent procaine) in Table VI.

The immediate postoperative results indicated in Table VII reveal the unusual high incidence (7 per cent) of deaths in the Cook County Hospital as

TABLE VI. ANESTHESIA EMPLOYED AT OPERATION

Local (1% procaine)	100
Local and ether	3
Local and ethylene	4
Local and cyclopropane	2
Nitrous oxide	17
Nitrous oxide, oxygen and cyclopropane	1
Nitrous oxide and ether	70
Ethylene	26
Ether and ethylene	4
Ethylene and cyclopropane	4
Cyclopropane	24
Spinal	28
Sacral block	6
Continuous caudal	7
Intravenous pentothal	1

TABLE VII. POSTOPERATIVE RESULTS

	COOK COUNTY HOSPITAL	MICHAEL REESE HOSPITAL	MT. SINAI HOSPITAL
Recovered	182	76	41
Died	14	0	0

compared to the private hospitals. This difference in mortality rates can be explained by the physical state and far-advanced stage of the pathologic condition in the patients who came to the Cook County Hospital. These patients are very often friendless and have no desire or incentive to live on as do the patients in private hospitals. This mental state although an intangible factor is an important one in considering mortality rates. An analysis of the pathology, operative procedure and anesthesia utilized in each patient who died, emphasizes those points to be discussed later as to preoperative preparation, prognosis in certain gynecologic pathology, the character of, and skill employed in the operative procedure as well as anesthesia and postoperative care (Table VIII).

Discussion

Statistical evidence shows a definite prolongation of the life span. When does old age begin or when is a woman too old to be operated upon are both relative, and answers may be varied and debatable. As Kosmak⁴ states, "old age is a relative term and may be designated when decline sets in. Some are more worth while and more competent and better able to take care of themselves at sixty than others at forty. Therefore it would be preferable to measure old age not by years but by competency, both physical and mental."

The question of surgical risk in the old woman has not been properly answered. It was assumed that the elderly individual was unable to tolerate anesthesia or operative procedures. These assumptions have been disproved by the many instances of emergency surgery where the patient was no more disturbed than a younger patient (i.e., torsion of ovarian cyst) and of elective surgery insisted upon by the patient. Since individual experiences were limited, no concerted effort was made to differentiate those women who may be safe operative risks from those who may not be. There are certain general and local conditions which are determinative factors.

At the initial consideration of surgery in the aged, the life expectancy must be weighed against the mortality rate of the operation. The mental state of the patient and outlook in life are important, and here the psychologic effect of the surgeon's approach may determine whether the patient will be optimistic and courageous or feel the approach of her doom. This state of mind, although intangible, can be evaluated with a little time spent conversing with the patient. She objects to any great changes in her daily routine, and therefore all effort should be made, if possible, to adhere to her daily routine.

According to Thewlis,³ surgical procedures in aged patients present many peculiarities. These include constitutional changes, greater resistance to infection when the individual is in fairly good condition, and considerably lowered resistance to infection when the body is debilitated; with more severe surgical shock, slower reaction from the shock; there may be lessened power of repair, cardiac and respiratory degeneration, and increased danger from anesthesia.

Taking full cognizance of the above constitutional peculiarities of the aged, when surgery offers the best result in a certain gynecologic condition, it is evident that the following steps must be taken to make the patient prepared for the operative procedure. A painstaking physical examination is essential to establish proper oral hygiene and eliminate infected teeth; to determine the adequacy of the cardiac reserve and coronary artery sclerosis by roentgen and electrocardiographic studies. Brumm and Willius¹⁵ reported on 257 patients with severe coronary artery disease who underwent necessary surgical operations. The average age was 60.3 years, 32 patients had healed infarcts at the time; in 100 cases there was well-marked arterial hypertension; eleven patients (4.3 per cent) died of cardiac causes. Some observers wait for two or three months after an attack before operating on a patient.

In addition to the cardiovascular status study, respiratory tract examination, renal function evaluation by urinary secretions, and blood chemistry determinations and blood picture scrutiny are all important steps toward making the decision, whether surgery may be considered reasonably safe. When a pathologic condition is found, an opinion as to the seriousness of the medical condition may be sought from a competent internist. We have already learned that hypertension without serious cardiac complication does not add much to the hazards of operation. Eighty per cent of the series studied had hypertension and probably a certain number would be benefited, since 73 per cent had some form of pelvic herniosus. The question of anesthesia in hypertensive patients comes up for consideration. Local, regional or low spinal anesthesia is well tolerated. In cardiopaths, ether-anesthesia can be used, while spinal is best avoided, although local may be employed.

Pulmonary emphysema and fibrosis and chronic bronchitis may favor the development of postoperative pneumonia; however, with serious pulmonary impairment, local or regional anesthesia may be best. In some cases cyclopropane or ethylene with oxygen may be used. Postoperative oxygen inhalation and frequent changing in position as well as early rising from bed are desirable procedures.

Kidney function should be tested in every case. A simple measure is the concentration test. If the specific gravity of the urine rises above 1.020, the kidney function is fairly adequate; if it remains between 1.015 and 1.020, there is impairment of renal function. Specific gravity that remains below 1.015 indicates serious renal damage. Determination of the urea nitrogen of the blood gives further information.

A complete blood count should be carried out preoperatively, since secondary anemia is common in old women. These hypochromic secondary anemias can be readily remedied. The general nourishment may be augmented by iron and the vitamins, especially the B complex. Transfusions may be employed to overcome anemias in urgent cases, as well as to increase the proteins of the blood.

Preoperative sedation must not be too great, since older individuals are readily depressed, and respirations become very slow, therefore barbiturates are preferable to morphine. Also, liver function being decreased, there is a decreased excretion of drugs, and therefore they are retained longer and have an accumulative effect. Intravenous pentothal is not considered safe.

Local (procaine) anesthesia is the most desirable anesthetic because it is the safest and is well tolerated by old people. Combination of pudendal block and local infiltration will allow the performance of any vaginal operation. Of the inhalation anesthetics, cyclopropane or ethylene with oxygen come next, then nitrous oxide and ether. Ether is well tolerated by cardiopaths.

The operative procedures must be rapid, precise, with little trauma or shock-producing manipulations. If proper hemostasis is accomplished with accurate approximation of tissue without strangulation, healing occurs readily. Vitamin C is believed to be of aid in the healing of the wounds.

Postoperative complications that occur with particular frequency among old patients are local wound infections, bronchopneumonia, urinary tract infections, thrombosis of the peripheral veins, and pulmonary embolism, cardiac infarction, and psychoses. Early mobilization of the patient is one of the best means of preventing most of these untoward events. The position of the patient in bed should be frequently changed, and she should be compelled to flex and extend her legs at frequent intervals. She should be allowed out of bed at the earliest possible moment. It is of interest to call attention to the fact that early ambulation postoperatively was first started among old patients, and now is becoming more generally used in all postoperative patients. Early postoperative ambulation has definite advantages, as determined by personal observations and by observations of others.¹⁶ Steinhart¹⁶ reviewed the literature and studied a small controlled postoperative series.

The mortality rate in old people treated surgically is higher than in young people; in view of the pathology and the senile changes present. Since the risk is greater, the individual patient must be thoroughly studied, as discussed above. If conditions allow, proper preparation may decrease the risk of surgery. Sanders and Sellers¹⁷ report a gross fatality rate of 1.8 per cent in 1,000 gynecologic operations in women of all ages. Sanders,¹⁸ in a later series of 500 patients, had a 0.2 per cent rate. In 6,022 operations performed on the gyne-

TABLE-VIII. BRIEF RÉSUMÉ OF DEATHS

NAME	AGE (YEARS)	CLINICAL OR PATHO- LOGIC DIAGNOSIS	OPERATION ANESTHESIA	DAY AND CAUSE OF DEATH
M. K.	74	Procidentia uteri	Vaginal hysterectomy. Anterior and posterior plastic. Ether and nitrous oxide	Nine hours postopera- tive—shock
B. C.	65	Procidentia uteri; leu- coplakia of cervix	Vaginal hysterectomy. Local	3rd day postoperative; pulmonary embolus, bronchopneumonia
K. M.	70	Adenocarcinoma of left ovary	Left salpingo-oophorec- tomy. Ether-nitrous oxide.	22nd day postoperative. Sepsis
S. W.	60	Inoperable adenocarci- noma of ovaries	Exploratory, biopsy of mass; ether-nitrous oxide	28th day postoperative. Sepsis; pyelitis
C. D.	67	Procidentia uteri; hemi- plegia 216/110	LeFort perineorrhaphy. Local	3rd day postoperative. Hypostatic pneumonia
N. C.	68	Large papillary cystade- noma of ovaries, arteriosclerosis, myo- carditis	Subtotal hysterectomy; bilateral salpingo- oophorectomy. Spinal	65th day postoperative. Decompensation of heart; terminal hypo- static pneumonia
J. S.	73	Large ovarian cyst with abscess	Laparotomy; incision and drainage. Nitrous oxide	38th day postoperative. Phlebitis of left leg; sepsis
E. N.	78	Diabetes; procidentia uteri	LeFort. Local	13th day postoperative. Pneumonia
A. B.	73	Procidentia uteri; hyper- tension 208/120	Vaginal hysterectomy; perineorrhaphy. Ni- trous oxide.	7th day postoperative. Uremia
B. S.	76	Procidentia uteri; ulcer of cervix; leukoplakia; chronic myocarditis	Vaginal hysterectomy; anterior and posterior plastic. Local	7th day postoperative. Sepsis
G. W.	70	Infiltrating squamous cell carcinoma of ure- thra; inguinal gland metastasis	Radical vulvectomy. Local	18th day postoperative. Sepsis
C. B.	79	Procidentia uteri; hemi- plegia	LeFort. Local	Discharged on 12th postoperative day; no home; remained in hospital and died on 40th postoperative day of hypostatic pneumonia
A. B.	68	Anaplastic carcinoma of ovaries	Exploratory; biopsy of omentum. Metastases to liver and peri- toneum. Spinal	39th postoperative day. Progressive downhill course
M. C.	70	Torsion of right ovarian cyst; carcinoma of rec- tum; fibroids of uterus; arteriosclerotic myo- carditis	Subtotal hysterectomy; bilateral salpingo- oophorectomy. Spinal	1st postoperative day. Cardiac failure

eologic service of the Cook County Hospital, Greenhill¹⁹ found a mortality rate of 3.5 per cent. At the Mayo Clinic,²⁰ in the years 1939 and 1940, 1,364 operations were done on 1,204 patients aged 65 years or over, with an operative mortality of 9 per cent. In those aged 65 to 74, the mortality was 8 per cent, in those 75 to 79, it was 13 per cent, and in those over 80, it was 35 per cent. In operations for prolapse of the uterus in 441 patients of all ages, the Michael Reese Hospital²¹ mortality rate was 1.6 per cent. The mortality rate in the 313 patients (Table VIII) reported was 4.5 per cent;

all deaths occurring in the Cook County Hospital patients. The difference in mortality rates is very striking, and definite reasons can explain it. The seriously ill and poorly nourished women with relative avitaminosis are more common in a public hospital like Cook County than in any private hospital. Thus, again the significance of the proper preoperative preparation of the patient is emphasized. The operative mortality rate in the old gynecologic patients is double (7.6 per cent) that of the series of all ages (3.5 per cent) at Cook County Hospital (Greenhill¹⁹). In analyzing the 14 deaths, the causes of death indicate that with our present chemotherapy and more available blood for transfusions, the mortality rate would have been decreased today. Fifty per cent of the deaths were due to sepsis. Only one death was due to postoperative shock and, in this instance, a 74-year-old woman was subjected to ether anesthesia. Embolism produced death only once. Cardiac failure accounted for two deaths, uremia for one, pneumonia for one. The far advanced anaplastic carcinoma of the ovaries with peritoneal carcinomatosis was the cause of one of the deaths rather than the surgical procedures (Table VIII).

Conclusions

1. Gynecologic surgery may be performed in old women (past 60 years) under urgent, imperative, or elective conditions with proper preoperative precautions, selection of anesthesia (especially local), careful, meticulous operative procedures, and proper postoperative care.

2. The higher mortality rate in older people was due to sepsis, shock, embolism, pneumonic infections, uremia, cardiac failure, but also due to the higher incidence of malignancies. With chemotherapy and blood transfusions, the most common operative complication may be combated.

3. Hypertension without marked cardiac damage is no great hazard. It may be improved by overcoming the partial ureteral obstruction and its resultant effect on the kidneys, in the correction of pelvic herniosus with the prolapsing uterus.

4. The relief experienced by an old woman with procidentia with good life expectancy more than balances the risk involved in the surgical care, thus adding a happy comfortable life to her years.

I am indebted to Doctor S. R. Lash and Dr. P. Grossbard for their aid in reviewing some of the patients' records.

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30 N. MICHIGAN AVENUE

STRESS INCONTINENCE IN THE FEMALE*

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URINARY incontinence in the female may arise from a variety of causes. It may be associated with congenital defects, with neurogenic abnormalities, or with trauma, usually incident to parturition. Such trauma may result in fistulas, in destruction of the urethra, or in herniation, i.e., urethrocele and/or cystocele. However, examination of the incontinent patient may reveal little or no external evidence of perineopelvic damage. And conversely, a large cystocele, a protruding urethrocele, even complete prolapse, may exist and the patient remain continent—sometimes to become incontinent after the pelvic floor is repaired.

This study is a consideration of the various factors concerned with the involuntary escape of urine through the intact urethra, and their treatment. Incontinence associated with obvious etiologic factors such as fistulas, nerve lesions, and congenital anomalies will not be considered. The actual urine loss may vary from only a few drops at the time of sudden increase in intravesical or intra-abdominal pressure to complete incontinence, even when recumbent. Complete incontinence is rarely encountered, but partial incontinence brought on by sneezing, coughing, or straining is all too common. It is to this type of incontinence that the word "stress" is applied.

A lack of uniform interpretation of perineopelvic anatomy still exists. Even the physiologic process of micturition and the pathologic physiology involved in incontinence are imperfectly understood. Unanimity exists only in the observations that this type of incontinence is frequently encountered in middle-aged multiparas, that it is an embarrassing, unpleasant incapacity, and that, although many operations have been devised, the treatment is often unsatisfactory. It is remarkable that, although the methods of treatment vary widely in both anatomic and physiologic approach, the end results have all been similar. Approximately 80 per cent of the patients are cured by any one of the many procedures advocated. Our study will attempt to explain why various types of repair meet with similar success.

Confusion and misunderstanding arise from the multiple terminology of a given anatomic structure; thus, the external voluntary urethral sphincter is variously known as the sphincter urethrae membranaceae, the sphincter urogenitalis, the compressor urethrae, the constrictor urethrae, the deep transverse perineal muscle, and the muscle of micturition. Some authors consider the sphincter urethrae membranaceae and deep transverse perineal muscle as separate entities, while others consider them as one and the same. We shall refer to this structure as the external urethral sphincter. These muscle fibers lie between two connective tissue sheets, and the entire formation which we will

*Presented before the Central Association of Obstetricians and Gynecologists, Fourteenth Annual Meeting, Chicago, Ill., Sept. 19 to 21, 1946.

refer to as the urogenital diaphragm is also termed the urogenital trigone, or the triangular ligament.

Then there is the musculofibrous tissue extending from the pubis to the cervix. It is referred to as the median fibers of the pubococcygeal portion of the levator ani, as the pubocervical fascia, as the pubocervical muscle sheet, vesicovaginal fascia, and as the pubovesicocervical sheath or fascia. We shall refer to this tissue as the pubovesicocervical fascia.

One author uses one appellation, another an entirely different one, and the reader becomes more and more lost. This confusion in terminology is a reflection of lack of uniform anatomic understanding. The structures that one investigator describes may not be apparent to another, or may be interpreted differently and called by another name. Further difficulty arises from the fact that fibers from several different structures are fused in the region of the urethra. We shall see that fibers from the pubovesicocervical fascia, the urogenital diaphragm, and the pubococcygeus form a single layer around the urethra.

The anatomic findings of cadaver dissection differ greatly from those demonstrable at the operating table. Likewise, the structures revealed by dissection of the perineum of the nulligravida differ from those of the multigravida. Curtis, Anson, and Ashley¹ have contributed a great deal to a rational understanding of pelvic structures. In addition should be mentioned the magnificent illustrations of Max Brödel² and the anatomic contributions of Johnston,³ Davies,⁴ Kennedy,³⁰ and others.

The bladder and urethra are surrounded by a loose areolar tissue which is an extension of the endopelvic fascia. This periurethral tissue is condensed on the ventral surface to fix the urethra and vesical neck to the undersurface of the symphysis pubis, while on the dorsal surface it becomes continuous with the pubovesicocervical fascia. Three smooth muscle layers are described in the urethra, an inner and outer longitudinal, and a middle circular. These layers are continuous with the bladder musculature. At the vesical neck the muscle is thickened and somewhat differentiated into a set of interlocking loops and circular fibers (Van Duzen and Looney⁵), referred to as the internal urethral sphincter, but also called the sphincter vesicae or the lissosphincter (Martius⁶). The fibers of this involuntary sphincter muscle pass in an oblique direction and extend into the fibrous sheath between bladder and vagina, as well as into the vagina. A strong group of longitudinal muscle fibers arise on the posterior bladder wall in the area between the ureteral orifices and pass downward, through the internal sphincter, to intermingle with the longitudinal fibers of the urethra. This muscle, the trigonalis, was well described in the male by Young and Wesson⁷ and plays a most important role in the physiology of micturition. The mucosa of the urethra is thrown into longitudinal ridges which make marked dilatation possible without injury. Between mucosa and muscularis is a cavernous vascular submucosa, the erectile tissue, or corpus spongiosum of the urethra.

As the urethra penetrates the three muscle layers of the pelvic outlet, fibers from each of these muscular layers become intimately associated with the

urethra. These layers consist of voluntary striated muscle, with their fascial coverings. From within outward they are known to us as the pelvic diaphragm, the urogenital diaphragm, and the superficial diaphragm. The superficial diaphragm is divided into three distinct bundles, the bulbocavernosus, the ischio-cavernosus, and the superficial transverse perineal muscle.

The bulbocavernosus is a musculofibrous sheath investing the vestibular mass of erectile tissue that lies in each labium majus. It arises from the posterior perineal body and divides into two superficial portions, one inserting in the corpus cavernosus of the clitoris with a fascicular band crossing the body of the clitoris, and a deeper portion that inserts into the urethra (Davies⁴).

The urogenital diaphragm consists of the external urethral sphincter and its two layers of fascia. These fibers arise from each side of the inner surface of the ischiopubic ramus, and pass medialward to insert in a median raphe, passing above and below the urethra, as well as supplying fibers to the urethra, vagina, and rectum (Fig. 1).

In the region subjected to perineal surgery, the urogenital diaphragm and the inner margin of the pelvic diaphragm (pubococcygeus) are in apposition, giving rise to the familiar muscular band so readily felt on vaginal examination, and usually referred to as the levator pillar or pubococcygeus. According to Curtis, the major part of this band is actually derived from the urogenital diaphragm, but through common usage this surgical entity is so often called the levator. We will refer to it as the pubococcygeus. It will thus be seen that median fibers from the pubococcygeus also reach the urethra, the vagina, and the rectum, and descend upon each of these structures, blending with the intrinsic muscular coat. Thus, the urethra is separated from the vagina by a musculofibrous sheath which contains fibers from the pelvic, urogenital, and superficial diaphragms, as well as smooth muscle fibers from the internal sphincter. From a practical viewpoint, the levator ani and its fascia are closely inter-related with the perineal sphincters and, by fixating the pelvic diaphragm, the levators synergize and coordinate the activity of the sphincters.

The structures which support the uterus at a higher level are also important. These thickenings of the endopelvic fascia, the cardinal ligaments, are blended with the adjacent structures. The innermost fibers of the cardinal ligaments pass to and around the cervix into the pubovesicocervical fascia.

The nerve supply of the bladder and internal sphincter consists of an intrinsic nerve plexus with outlying ganglion cells and fibers that have been shown to be capable of functioning after all other nerve fibers are destroyed. In addition, they receive sympathetic fibers from the hypogastric nerve (presacral nerve) and inferior mesenteric ganglion, and parasympathetic fibers from the second, third, and fourth sacral nerves by way of the pelvic nerves (nervi erigentes). The voluntary urethral sphincter and the associated voluntary pelvic and perineal muscles are innervated by the pudendal nerves (somatic) derived from the sacral (3 and 4) portion of the cord.

The physiologic mechanism of micturition involves the concept of the opening of both the involuntary and voluntary sphincters at an appropriate time. According to Denny-Brown,⁵ the lumbosacral segment contains all of the nervous mechanism necessary for micturition except that which decides whether its occurrence would be appropriate to the environment. The latter is provided by the higher centers. In the normal female the internal sphincter alone can retain urine within the bladder. The sphincter is closed, but not in a state of con-

tinuous contraction. If, however, it is gradually distended, it will contract—the force exerted being proportional to the degree of distention. Relaxation of the internal sphincter and urethra is brought about by contraction of the bladder, the arching trigone bundle opening the passage by its down pull (Van Duzen and Looney⁵). As the bladder is emptied, the sphincter again gradually returns to its closed state. This reciprocal bladder-sphincter mechanism is apparently dependent on the intrinsic nervous plexus. Division of the presacral nerve (sympathetic) will cause paralysis of the trigone muscle and delay in starting the stream, because now increased intravesical pressure alone must open the sphincter. Royston and Rose⁹ have stressed the importance of repair of the trigone muscle in those patients who have suffered injury to that structure. Van Duzen³¹ advocates presacral neurectomy in obstinate cases of stress incontinence in which other measures have failed.

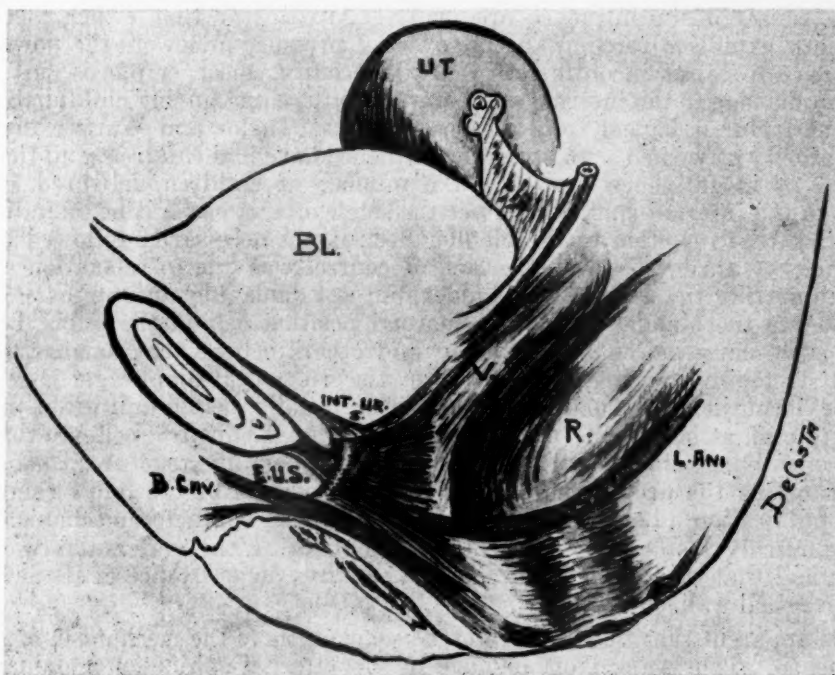


Fig. 1.—The external urethral sphincter (E.U.S.) and its relationship to adjacent structures: *B.Cav.*, bulbocavernosus; *BL.*, bladder; *INT. UR. S.*, internal urethral sphincter; *L.ANI*, levator ani muscle; *R.*, rectum; *UT.*, uterus; and *V.*, vagina.

The external sphincter is a compact, quick-acting muscle that is capable of rapid reflex action. Ordinarily it is relaxed, but is brought into play when there is a sudden rise in intra-abdominal and, hence, intracystic pressure. It has been shown that a sudden, moderate rise in intravesical pressure will not force open the normal internal sphincter, hence the external sphincter may not be necessary unless the internal mechanism is weakened or the rise in pressure is marked. With internal sphincter damage, the external sphincter is usually sufficient to preserve continence. However, damage to the latter removes the second barrier and a rise in vesical pressure associated with effort, coughing, sneezing, laughing, even quick motions, may be followed by urinary loss.

At times the damage to the sphincter mechanism may be manifested as a delay in the reflex reaction of the voluntary muscle, the incontinence occurring only at the very onset of increased pressure. Later control causes adjustment,

so that there is no further leakage. This type of incontinence is evident, particularly when the bladder is partially distended. Coughing, sneezing, or moving suddenly causes incontinence, but continuation of the same process does not cause repeated urine loss.

The third barrier, the superficial pelvic diaphragm, is also brought into play reflexly at the same time as the external sphincter.

Continence is further maintained by the slight mechanical barriers imposed, consisting of the abundant mucosa in folds and the erectile tissue of the submucosa, both structures narrowing the lumen. Angulation of the urethra at the vesical neck is believed by Taylor and Watt¹⁰ and others to provide additional resistance. The excellent studies of Barnes,¹¹ however, do not confirm a constant relationship between angulation and incontinence, but demonstrate that a wide variation in urethral angulation occurs in continent patients.

The causes of incontinence are many. Any factor that either increases the urinary expulsive force or the intravesical pressure or lowers the powers of resistance can cause incontinence. Until recently, most emphasis has been placed on damage to the internal sphincter. That trauma during childbirth is an important factor is logical from the observations (Taylor and Watt¹⁰) that the great majority of women with stress incontinence have had children, and that the incidence of incontinence rose with the number of children delivered. That damage to the internal sphincter is not the sole cause, if cause it be, is indicated by the fact that resection of the bladder neck is not necessarily followed by incontinence. Watson¹² believed the lack of control was due to relaxation of the fascia supporting the neck of the bladder, but not damaging the sphincter itself. By replacing the bladder neck to its normal position behind the pubis, he was able to cure many patients. Johnston³ and others believe that damage, either through stretching, tearing, or necrosis, of the urogenital diaphragm is responsible for incontinence, the internal sphincter usually being uninjured during childbirth and, at best, being a small, weak muscle. Kennedy¹³ believes that the incontinence is associated with damage to the supporting structures plus adhesions distorting the urethra and fixing it to the margin of the pubic rami. In a later publication (1941), Kennedy¹⁴ adds that the sphincter mechanism can be satisfactorily restored by plicating and replicating the undersurface of the urethra, and that the sphincter mechanism requires no assistance of the levators and the vaginal wall.

It is apparent that there are different concepts as to the mechanism of stress incontinence. They vary from damage to the internal sphincter to damage of the external sphincter and the supporting structures of urethra and bladder. It seems probable that incontinence is not the result of any one cause, but may result from one or another cause, or from several. It is further probable that the damage incident to parturition involves in varying degree, by stretching and tearing, all the structures associated with the bladder and urethra. The shutoff mechanism can apparently withstand many insults without breakdown, and the final outcome depends not only on the damage inflicted, but also on the constitution of the tissues subjected to the trauma.

There are many generic types of operations which have been advocated and used in the treatment of stress incontinence. One of the earliest to meet with success was advancement of the urethra as devised by Pawlick, and later modified by Dudley.¹⁵ Torsion of the urethra was advocated and practiced by Gersuny, and later modified and combined with advancement by Ries. Both the Dudley and Ries operations are still described in detail in modern operative gynecologic textbooks (Crossen and Crossen¹⁶). In 1913, Kelly¹⁷ advocated shortening the internal sphincter with a mattress suture, and to this day this operation is probably the best known and most frequently used. Watson¹² advocated care-

ful imbrication of the fascial supports of the bladder, restoring the bladder to its normal position behind the pubis and correcting the cystocele. Bissell¹⁸ utilized the muscular layers of the vagina to support urethra and bladder neck. Frost¹⁹ mobilized the urethra and bladder, plicated these structures without tension, and re-enforced this repair by strips excised from the anterior vaginal wall sutured under the vesical neck to the undersurface of the symphysis. The use of fascial strips or fascia and muscle strips derived from anterior abdominal wall muscles to produce a sling under the urethra has been advocated by Goebell,²⁰ Stoeckel,²¹ Miller,²² Aldridge,²³ and others. Deming²⁴ transplanted the gracilis muscle. Lowsley²⁵ imbricated the bulbocavernosus above the urethra. Martius²⁶ transplanted the bulbocavernosus beneath the urethra. Taussig²⁷ transplanted strips of the levators beneath the urethra. Berkow²⁸ advocated urethral advancement and approximation of the bulbocavernosus and pubococcygeus beneath the urethra. Kennedy²⁹ stressed the importance of subpubic adhesions and distortions of the urethra. In his operation, these adhesions are freed, the urethra plicated in the midline to prevent further adhesions forming, and the "sling fibers" joined below the urethra.

In analyzing the various procedures employed, we note that one of several mechanical changes is made: (1) the urethra is lengthened or twisted, thereby decreasing its lumen and, by stretching, increasing its tone; (2) the urethra and/or bladder are returned to their normal position behind the pubis, re-establishing the urethrovesical angle and tightening the fascial support; (3) the musculature of the bladder neck and/or urethra is plicated, decreasing the lumen and strengthening the fascial support; or (4) a musculofascial sling is placed below the urethra, which (a) by mere pressure narrows the canal, (b) provides additional support for the urethra, and (c) may function by voluntarily contracting the urethra when stimulated, and (d) tightens the fascial supports. No matter what the explanation for success given by the author, *all procedures have in common the tightening of the fascial planes through which the urethra and vagina pass.* This even applies to advancement or torsion of the urethra, because the fibers from the levators, urogenital diaphragm, and superficial diaphragm, even the internal sphincter, are stretched by these procedures. The fascial supports of the pelvic floor are further tightened by the customary procedure of repairing cystocele or rectocele, if present.

In the paraurethral fixation operation described by Berkow, the urethra is advanced and slightly angulated, thereby narrowing the lumen, increasing the length of the urethra, and increasing the tension of all the fibers it receives from adjacent structures. The pubococcygeus muscles are approximated below the urethra. Further support is given by uniting the two bulbocavernosus muscles as a second layer, thus creating a strong anterior muscular support. With the colpoperineorrhaphy the fascial layers are further tightened. Imbrication of urethra and/or bladder neck is not employed. Actually, imbrication, including Kelly's internal sphincter plastic, can be considered as merely another method of tightening the supporting fascia.

Technique

The patient is placed in lithotomy position and the labia minora are sutured laterally for exposure. A traction suture is placed just below the clitoris. A second traction suture is placed four to five centimeters below the external urinary meatus. The mucosa of the vestibule is then picked up by two Allis forceps on either side of, and one to two centimeters below, the urinary meatus.

Sustained traction on the two Allis forceps and on the two traction sutures outlines a quadrilateral area which includes the vestibule and anterior vagina, and brings these structures into a single plane. A diamond-shaped incision is made outlining this quadrilateral area (Fig. 2). A second incision through

the mucosa is made encircling the external urinary meatus. This is kept 0.5 cm. from the orifice to leave an ample cuff for subsequent suturing. That portion of the mucosa contained between the two incisions is removed by sharp dissection, thus denuding the entire area (Fig. 3).

The urethra is picked up by toothless forceps and pulled upward toward the clitoris. This puts the urethral wall under tension, and makes the urethral dissection easier. The urethral wall is dissected free from the underlying structures (Fig. 4). This is accomplished by "scraping" the tissues away from the urethral wall by means of a sharp scalpel. This procedure is carried back along the urethra toward the bladder until the urethra has been freed sufficiently to allow the dissected external meatus to lie just under the clitoris without traction. Such a dissection by "scraping" seems hazardous, but there has been no urethral injury in any of our patients. We believe that urethral injury is more likely to result when a catheter is used. The "scraping" dissection results in moderate and continuous venous oozing, but experience has shown that hemostasis is unnecessary and time-consuming at this point. Satisfactory hemostasis is always obtained subsequently by the sutures which are used to unite the pubococcygeus and bulbocavernosus muscles.

The urethra is now anchored just below the clitoris by three interrupted mattress sutures. Chromic catgut No. 00 is used throughout the operation. This upward placement and suturing of the urethra brings into view the pubococcygeus muscles which are now united in the midline beneath the urethra by two to four interrupted sutures (Fig. 5). The bulbocavernosus muscles are then united in the midline, thus completing the second layer of sutured muscles which hold the urethra upward (Fig. 6). The cut edges of the mucosa are united to the cuff about the urethral orifice by mattress sutures. Several sutures are also used to unite the mucosa in the midline (Fig. 7).

An indwelling catheter is inserted and remains in place for five to seven days. It is used because the postoperative edema about the external urinary meatus makes catheterization difficult, even when attempted by someone experienced with this type of operation. Resultant trauma might tear out the delicate superficial sutures and thus undo the entire operation.

The operation here described and as originally described by Berkow is not difficult and can be quickly performed. It may be carried out as a single procedure, or may be combined with a cystocele repair, vaginal hysterectomy, or both. The vaginal hysterectomy and/or cystocele repair should be performed first and followed by the paraurethral fixation. Colpo-perineorrhaphy, when indicated, should be performed last.

Convalescence is short and usually uneventful. The patients are permitted out of bed after the first forty-eight hours. They may be ambulatory, even though the indwelling catheter is in place. This can be accomplished by disconnecting the catheter from the suction apparatus to which it is usually attached and corking the free end of the catheter.

Para-urethral fixation has been performed 33 times by us during the past five years. The 33 patients ranged in age from 23 to 82 years. Twenty-nine were parous women, and the stress incontinence was obstetric in origin. Four were nulliparous, and the two failures in our series both occurred in this group. Patients were followed for periods ranging from five to fifty-four months postoperatively.

Preoperative examination showed that 17 patients had a urethrocele. In the remaining 16 patients, stress incontinence was present, but no definite urethrocele was demonstrable. Of the entire group, 13 had a cystocele, five had second or third degree uterine prolapse, four had complicating fibroids of the uterus, and two had cervical and uterine polyps.

Fig. 2.



Fig. 3.

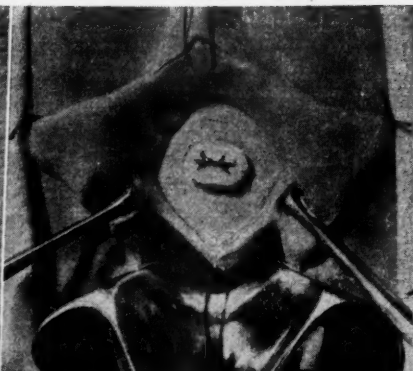


Fig. 4.



Fig. 5.



Fig. 6.



Fig. 7.



Fig. 2.—The labia minora have been sutured laterally, and traction sutures have been placed below the clitoris and in the anterior vaginal wall. The quadrilateral area of the vestibule and anterior vaginal wall is thereby outlined. The diamond-shaped incision and encircling urethral incision have been made.

Fig. 3.—The vestibular mucosa has been excised.

Fig. 4.—The urethra has been carried anteriorly and freed from the underlying tissue.

Fig. 5.—The pubococcygeus muscles have now been approximated. The needle has been inserted through the bulbocavernosus for the placement of the first suture in the second layer.

Fig. 6.—The bulbocavernosus muscles have been united beneath the urethra.

Fig. 7.—The mucosa has been united by the addition of several mattress sutures, thereby completing the operation.

Paraurethral fixation was performed in all 33 patients. This was the only operative procedure in 13 women who had no complaints other than stress incontinence and no complicating pelvic pathology. Multiple operative procedures were performed in the remaining 20 women. These included 14 anterior colporrhaphies and 11 colpoperineorrhaphies, seven vaginal hysterectomies, two abdominal hysterectomies with bilateral salpingo-oophorectomy in each, and two polypectomies.

An indwelling catheter was used postoperatively in each instance, for an average length of time of six days. There was no morbidity referable to this procedure, and bladder function following removal of the indwelling catheter was normal in seventeen. Catheterization was necessary once in 13 patients, twice in two, and six times in one patient.

The average hospital stay for the 13 patients who had paraurethral fixation only was ten days, while the average hospital stay for the entire group was twelve days.

There was no postoperative morbidity in 26 patients, while seven ran a febrile course. One patient, a 50-year-old para ii, developed fever and cough on the third day following abdominal hysterectomy, bilateral salpingo-oophorectomy, and paraurethral fixation. These complaints persisted for one week, and were probably due to a pulmonary infarct, although neither the physical findings nor roentgenography were conclusive. This patient was discharged on the thirteenth postoperative day. Her cough persisted for two months, during which time there was a continuation of the stress incontinence. As the continuous hacking cough disappeared, her bladder symptoms disappeared, and, at follow-up examination three months later, she was completely continent.

Postoperative thrombophlebitis occurred once. The patient was a 39-year-old para v who had urethrocele, cystocele, rectocele, and multiple uterine fibroids. A vaginal hysterectomy, anterior colporrhaphy, and posterior colpoperineorrhaphy followed by paraurethral fixation resulted in a febrile convalescence lasting twenty-three days because of thrombophlebitis of the left leg.

A final operative complication is of interest because it emphasizes the importance of careful preoperative diagnosis. The patient, a 52-year-old para iii, complained of marked incontinence for the past two years. It began immediately following a total abdominal hysterectomy to remove uterine fibroids. Loss of urine followed almost any type of activity, but never occurred when lying down. There was definite loss of urine from the urethra on straining or coughing. Careful urologic examination, including cystoscopic examination of the bladder, revealed no abnormality. Postoperatively, incontinence persisted after removal of the indwelling catheter. Cystoscopic examination four weeks following the paraurethral fixation disclosed a small vesicovaginal fistula. This was repaired five weeks after the first operation with good results. It seems improbable that the vesicovaginal fistula resulted from the paraurethral fixation; for the area of the bladder involved in the fistulous tract was at a considerable distance from the urethra. It is much more likely that the vesicovaginal fistula followed the abdominal hysterectomy, and that our preoperative diagnostic methods failed to reveal its presence. If the fistula had been detected, as it should have been, it would have been corrected and the paraurethral fixation then performed.

All patients were examined four to six weeks postoperatively. At this early date, about one-half still have some degree of impairment. This decreases gradually during the next three to four months. Examination of the 33 patients in this series at the end of four months showed complete continence and urinary control in thirty-one. Apparently considerable time must elapse to achieve complete success with this operation. The resultant scar formation and tissue

retraction take twelve to sixteen weeks. Likewise, time is a factor in the development of urinary control. It is essential to advise such patients that complete continence may not be obtained for several weeks. Failure to inform them will lead to some unhappiness for the first few postoperative weeks.

The patients must also be informed of the resulting change in the direction of the urinary stream. Following paraurethral fixation, the dislocated external urinary meatus causes the stream to be more horizontal than normal. This may result in wetting and annoyance. It can be completely overcome by tilting the body forward during micturition. The patient must be forewarned and taught to lean forward while voiding.

Two patients developed cystitis and recurring stress incontinence twelve and twenty-four months following paraurethral fixation. Both responded to chemotherapy plus urethral dilatation and urethral massage. A Walther urethral dilater is inserted into the urethra, and the dilated urethra is massaged rather vigorously through the anterior vaginal wall. Dilatation with massage is done twice weekly for two to four weeks, and apparently helps to restore normal tissue tone. This procedure also seems to be of value during the period of late convalescence, i.e., six to twelve weeks postoperatively. Dilatation with massage apparently speeds up the return to complete urinary control. It was carried out in six patients with beneficial results.

One patient became pregnant and has delivered two full-term babies without the recurrence of stress incontinence. When last seen on June 21, 1946, she was again pregnant, but completely continent.

There were two complete failures in this series of 33 patients. One was an 82-year-old nullipara who had anteroposterior suturing following total colpocleisis rather than side to side closure. The resultant pull on the urethra produced stress incontinence. Paraurethral fixation was performed, but gave absolutely no relief of the distressing symptoms.

The second failure occurred in a 48-year-old nullipara. This patient had been treated for incontinence over a period of twelve years with varying degrees of success. Some four years ago the Kelly operation was performed which relieved her symptoms for a few months. Estrogenic substance in varying dosage also afforded temporary relief. Urologic examination failed to disclose any abnormality, and gynecologic examination was not significant. The patient was depressed, frustrated, and unhappy. She was not willing to consult a psychiatrist, but it was hoped that paraurethral fixation would solve her difficulties. As with the Kelly operation, she received relief for a period of about three months. It is believed that her incontinence is on a psychosomatic basis. She should not have been subjected to surgery without a thorough psychiatric workup. We were a bit too optimistic.

Summary and Conclusions

1. The anatomy of the female bladder, urethra, and associated structures is described.
2. The physiology of micturition is discussed.
3. Obstetric injury to the urethra and supporting structures is the commonest cause of stress incontinence.
4. Operations devised to correct stress incontinence are evaluated. All these procedures have in common the tightening of the fascial planes which surround the urethra, together with reduction of the urethral lumen.

5. Paraurethral fixation was carried out in a series of 33 patients suffering from stress incontinence.

6. It was completely successful in 31 patients, the only two failures occurring in women in whom the etiology of the stress incontinence was not obstetric.

7. Paraurethral fixation is a most satisfactory operation for the relief of stress incontinence following obstetric injury.

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PUERPERAL GYNECOLOGY*

A Report of Thirty Years' Experience With Gyneplastic Repair Operations Immediately After Childbirth

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SINCE October, 1916, when I performed my first operation for repair of old lacerations of the genitals during the puerperal period, I have been advocating the value of repair of old, new, or combined injuries caused by childbirth, and, since 1918, I have presented numerous publications¹⁻¹⁸ on this subject. During the same period, other authors,¹⁷⁻³³ either as a result of my work or independently, have reported on operations performed during the puerperium for repair of old or new injuries. Nevertheless, the fact remains that the majority of obstetricians are still hesitant to do this work, and continue to regard such procedures as "too radical" and perhaps dangerous. Since the benefits accruing from this type of obstetric care are so great in terms of improved general health, greater working efficiency, economic saving, and probable protection from cancer in later life, I feel that it is important to restate the salient points of this work and to bring the record of my personal experience and those of my colleagues at Mt. Sinai Hospital up to date.

Progress cannot be made in any field unless so-called radical procedures are tried and evaluated; every innovation is considered radical until it is proved by long experience to be safe and practicable. Science is constantly producing startling changes in our environment and habits. That which was considered a radical surgical procedure a generation ago can now be done in comparative safety, because of improvements in surgical technique and hospital care. Certainly, the procedures that I am advocating, which I have practiced consistently for thirty years, and my colleagues for a slightly shorter period, may be said to have stood the test of time and to have long ago passed the experimental stage. Time has not changed, but rather has strengthened my conviction that puerperal gynecology is feasible, safe, and of immeasurable value to the patient and should be universally adopted as an integral part of natal care.

Since our results over thirty years show conclusively that the hazards of childbirth are not increased by immediate repair operations (provided no surgical contraindications are present), since the technique has been well standardized and has proved practical in the hands of various obstetricians, and since the health and comfort of the patients are so greatly improved by these methods, at enormous saving both to the patients and to the community, it is difficult to see why puerperal gynecology has not been more generally

*Presented at the Fourteenth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Chicago, Ill., Sept. 19 to 21, 1946.

adopted. As far as the future welfare of the mother is concerned, it is relatively unimportant how cleverly the accoucheur has manipulated the delivery, if he has neglected to carefully examine the genitals and repair any lacerations that may be present.

I do not advocate the universal adoption of puerperal gynecology by untrained men. The student, the practicing physician, and even the specialist must appreciate the difficulties as well as the advantages of this type of obstetric care and train toward perfection of technique as in any branch of major surgery. Our interns are given this training as part of their curriculum; judgment, speed, and dexterity are developed with experience so that even extensive repairs are accomplished at a minimum of risk.

There is another aspect of the subject that must be mentioned: this concerns ethics and the obligation of the physician and surgeon to give his patients the best possible care he can provide at minimal expense. I have heard that some obstetricians object to the principle of puerperal gynecology on the basis that it reduces their income; they are afraid of losing another fee for performing a subsequent gynecologic operation. Some obstetricians also raise the objection that they cannot devote the additional time for this service, especially during the night. My colleagues and I have often performed complete repair operations in the early hours of the morning, and we feel that the satisfaction of knowing that the required work has been done has more than compensated for the sleep thus lost.

During the first few years when the technique was in an experimental stage, the repair of old injuries was done about a week after delivery, and was called "the intermediary repair operation." With improved technique and judgment derived from experience, the time between delivery and repair was gradually shortened; finally, the operation immediately after delivery became routine (unless there were specific contraindications) and the term "immediate intermediary operation" was used. My first report of surgical repair of cervical lacerations performed immediately after expulsion of the placenta was published in 1918.¹ Up to 1930, a distinction was made between repair operations for old injuries and those performed for new ones. During the ensuing years, the procedures were called "gyneplastic repairs."^{5, 7, 10, 11} Since 1931, I have used the term "puerperal gynecology"¹²⁻¹⁵ to cover the whole field of repair of new, old, and combined injuries caused by childbirth.

The record of our cases over this long period are indisputable proof in refuting certain charges which have been made against the advisability of performing gyneplastic repair immediately after childbirth. It was formerly considered dangerous to invade the birth canal after delivery for fear of producing hemorrhage and of introducing infection. These can be avoided by careful technique and by observing the same aseptic and antiseptic precautions as in any major surgical operation. It has been claimed that the tissues are so edematous, bruised, and distorted that it is impossible to differentiate between temporary and permanent disturbances, and that many of these operations are unnecessary because there may be complete restitution after.

childbirth. With experience, however, the lines of cleavage can be readily recognized and the various layers of tissues can be easily separated without tearing, and with less effort than in delayed gynecoplastic procedures. Any obstetrician who is also a gynecologist and has observed the end results of childbirth can prophesy in which cases the relaxation will be temporary and in which it will be permanent. It must be remembered that the degree of subsequent disability does not depend entirely upon the extent of relaxation or laceration. Hence, when future trouble is anticipated, a prophylactic repair of the cervix, a relaxed anterior vaginal wall (primary cystocele operation,⁶ or the repair of a relaxed perineum immediately after delivery is much more effective and practical than a later operation to "cure" a serious disability.

It used to be said that the lochia would interfere with healing of tissues, but our experience, and that of many other surgeons, have disproved this contention. The lochia does not interfere with healing unless infection is present or the sutures are so tight as to obstruct circulation and cut through the tissues or interfere with drainage. Another objection has been that the patients are more comfortable during the lying-in period when repair operations are not performed. This is undoubtedly true, but since they are incapacitated at this time, anyway, the additional discomfort is willingly borne in the knowledge that another operation or prolonged disabilities are avoided.

It is not within the scope of this paper to repeat the indications, which are self-evident, or all the details of the technique used which I have already reported in numerous articles. Few changes have been made in our methods, except in the choice of analgesia and anesthesia. Recently we have been using demerol (100 mg.) and seconal (1.5 to 3 grains) routinely toward the end of the first stage of prolonged labor. When the patient is in active labor and the cervix is dilated at least two centimeters, the dose is repeated as often as necessary. We use nitrous oxide and oxygen, with or without ether, for the anesthetic in many deliveries and repairs as well as local, spinal, or sacral anesthesia, according to the preference of the operator and the indications in the individual case. Continuous caudal anesthesia has certain advantages, but has been used in only a small series of cases in our hospital because the care demanded has precluded its use during the war years. Recently we have used low lumbar anesthesia in a large proportion of cases. The infants cry spontaneously, bleeding is minimal, and the uterus remains contracted and firm after its use. The injection of anesthetic solution should not be begun before the cervix is dilated or severe cervical lacerations will occur. Nevertheless, even proper timing will not entirely prevent cervical lacerations; these will occur in some cases with any type of anesthesia or with any method of delivery.

A few important points in the technique must be stressed. Repair immediately after the delivery has many surgical advantages. One anesthesia serves for both delivery and operation. Danger of infection and its attendant morbidity are reduced. It has been proved that bacteria multiply in the uterus within two or three days after delivery; usually they are innocuous, but sometimes become pathogenic. Immediately after delivery, the cervix can be pushed

down from above and pulled down to the introitus from below with ring forceps without much force and with little trauma, due to the complete relaxation and stretching of the supporting ligaments of the uterus and the dilatation of the vaginal canal. Before beginning the repair, the uterine cavity is swabbed with gauze soaked in tincture of merthiolate solution, while further pressure is exerted on the fundus. This maneuver stimulates the uterus to further contraction, cleans out the blood clots, fragments of placenta or membranes, and helps to sterilize the uterine cavity, cervical canal, and vagina.

Repair of the Cervix.—This is the most important feature of puerperal operations. Rarely is an intact cervix found, even after a slow, normal labor. Any new lacerations, regardless of size, extent, and number are repaired. If a submucous tear is present, as evidenced by puckering or localized depression, a typical trachelorrhaphy is performed to reunite torn muscle fibers and the vaginal mucosa. In suturing the cervix, it is important that no pockets or fistulous tracts remain along the line of suture, that the vaginal mucosa on the outer side of the cervix is smooth, so that no adhesions may form between the cervix and the vaginal wall, that the external os is not so tightly closed as to interfere with drainage, and that no gaping occurs at the angles of the cervical os. If there is a pouching of the anterior cervical mucosa, owing to a submucous hemorrhage, the excess tissue is removed with an egg-shaped incision (endocervicectomy), the blood clot is evacuated, and the edges are brought together with a continuous interlocking suture of 00 chromic catgut. This requires only a few minutes and prevents subsequent pronounced endotrachelitis, which is a frequent cause of leucorrhea and subinvolution of the cervix and uterus.

Cystocele.—The degree of suffering resulting from a cystocele is unrelated to its size. Many patients with very slight bulging of the bladder suffer more than those who have pronounced herniation. A cystocele or an urethrocele is a hernia and cannot be cured without careful and complete mobilization of the involved tissues. When excessive tissue is allowed to remain, the patient complains of a fulness and irritation, even though the fascial and muscular structures are firm and in good position. It has been found at subsequent deliveries that the vaginal wall has sufficient elasticity to compensate for tissue that has been removed. The idea that a good perineal body will take care of a sagging anterior wall, i.e., a cystocele and urethrocele, is fallacious and without proof.

Lacerations of the Vaginal Walls.—Careful examination of the vaginal walls is carried out after repair of the cervix is completed. Deep structures are brought into normal position by the use of continuous or interrupted chromic sutures in one or more layers, depending on the depth of the laceration. All pockets must be eliminated. All severely traumatized, thrombosed, or ragged tissue is cut away, the parts are brought together, and the free edges of the mucosa are then united by a continuous, interlocking No. 1 chromic catgut suture.

Rectocele.—The object of the operation for repair of a rectocele is to remove the scar tissue, to cure the hernia, and to replace the various layers of muscle and fascia in their proper positions. A prophylactic rectocele operation may be performed on patients with no external evidence of perineal lacerations who present definite signs and symptoms of a rectocele. This condition may be recognized immediately after delivery by pouching of the rectum through the thinned or torn rectovaginal septum. This practically never returns to normal, but can be cured by exposing the fascia according to a previously described technique.¹⁴ In repairing new perineal lacerations, episiotomies, or combined new and old tears, all severely traumatized, thrombotic, and scarred tissue is cut

away, the various anatomic structures are identified and sutured in layers as for the repair of a rectocele. Any old relaxations or lacerations of the perineum are thoroughly exposed and treated, regardless of primary tears.

Hemorrhoids.—If any edematous or enlarged hemorrhoids are present, the sphincter ani is dilated and the hemorrhoids are either incised and the blood clots expelled, or the hemorrhoidal area is removed, followed by suture with No. 00 chromic catgut. In many instances, clusters of hemorrhoids have been removed by a modified Whitehead operation, with excellent results.

The obstetric activity at Mt. Sinai Hospital for the last ten years is demonstrated in the accompanying tables which supplement those in my previous reports and bring our records of thirty years' experience with puerperal gynecology up to date. Table I shows the age of the mothers delivered between 1936 and 1946. Contrary to popular belief, there was not a greater proportion of younger mothers during the war years. In fact, the 30- to 39-year group show the greatest relative increase. There is great satisfaction in the knowledge that complete restitution of lacerated genital organs in the very young women has spared them many years of possible invalidism.

TABLE I. AGE

	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945	Total
Under 20	22	17	21	24	18	13	35	58	49	55	312
20-29	465	398	498	529	615	753	998	876	724	869	6,725
30-39	175	233	224	231	282	326	392	428	392	417	3,100
40-49	6	13	7	8	11	12	16	18	10	16	117
Total	668	661	750	792	926	1,104	1,441	1,380	1,175	1,357	10,254

TABLE II. PARITY

	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945	Total
i	359	380	417	425	530	665	870	772	539	680	5,637
ii	195	183	226	250	296	312	436	467	421	488	3,274
iii	73	66	72	85	71	100	92	105	149	135	948
iv	29	22	20	17	19	17	31	28	34	45	262
v	5	4	4	7	5	7	5	4	19	4	64
vi	2	3	3	5	2	1	1	2	6	4	29
vii	2	2	2	1	1		4	1	5	1	19
viii		1	3	1	1	1	2	1	1		11
ix	1		1	1	1						4
x	1		1								2
xi			1			1			1		3
xii	1										1
Total	668	661	750	792	926	1,104	1,441	1,380	1,175	1,357	10,254

Table II indicates that there is a predominance of primiparas, almost twice as many as secundiparas, and six times the number of tertiparas. That repair operations should be delayed until the childbearing period is passed is thus proved impractical, since so many women limit their family to one or two children. Since 1920, the performance of immediate repair operations has become almost a routine practice by our obstetric staff, and the number of repair for old injuries has therefore constantly decreased. When multiparas return for subsequent deliveries, the old scar tissue is cut away immediately after delivery and current injuries are repaired, as in the cases of primiparas.

Table III charts the types of deliveries which totaled 10,254 from 1936 to 1946. The number of maternity cases has increased with a corresponding increase in the number of gynecologic operations.

Episiotomies have been listed in Table IV with the types of operations because they include a repair procedure. Of special interest are the 2,191

operations performed on the cervix and the 335 hemorrhoidectomies. Our records for the entire thirty years total over 20,000 operations.

Table V reports the complications that we encountered during this period. Although the morbidity following immediate gynecoplastic repair operations is somewhat greater than that following deliveries in which no operation is performed, this has not constituted a serious problem. With adequate measures to control infection, proper surgical technique, and use of modern methods to avoid dehydration, distention, anemia, and other conditions contributing to postoperative illness, the maternal morbidity has steadily decreased from 23.5 per cent in 1353 cases, 1922-1929 to 4 per cent in 10,254 patients delivered 1936 to 1946. In calculating the morbidity rate, the standard set by the American Congress on Puerperal Infection, any elevation to 100.4° F. or over on any two consecutive days, not including the first twenty-four hours after delivery, is used. This is a fallacious standard, for many women who have been badly lacerated and poorly repaired may not have any rise in temperature, but the morbidity is self-evident.

Our morbidity and mortality has been lower than that reported by institutions in which no gynecoplastic operations were performed during the puerperal period. In fact, since 1930, *there has not been one maternal death* that could possibly be attributed to a repair operation.

TABLE III. TYPES OF DELIVERIES

	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945	TOTAL
Prophylactic and low forceps	468	350	453	546	662	710	973	902	783	942	6,789
Midforceps	42	93	80	43	28	95	108	98	50	45	682
High forceps		6	2	4	1		2	2	1	3	21
Version and extraction	25	37	20	16	25	38	22	41	11	10	245
Cesarean section	30	25	26	33	36	34	49	48	36	61	378
Scanzoni maneuver	4	14	28	39	57	55	85	62	52	69	465
Manual rotation			2			11	3		15	22	53
Breech extraction	22	27	21	35	45	50	66	54	35	43	398
Piper forceps									7	4	11
Spontaneous	77	109	118	76	72	111	133	173	185	158	1,212
Total Deliveries	668	661	750	792	926	1,104	1,441	1,380	1,175	1,357	10,254

TABLE IV. TYPES OF OPERATIONS

	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945	TOTAL
Episiotomy	470	441	547	590	674	734	1,231	934	908	911	7,440
Trachelorrhaphy	265	225	232	211	195	223	226	265	151	200	2,191
Perineorrhaphy	82	39	99	102	100	90	85	122	31	85	835
Repair of perineal lacerations	40	80	47	34	31	45	42	56	98	79	552
Repair of vault lacerations		54	73	20	38	37	35	31	12	28	328
Cystocele		4			1	14	16	20	1	4	60
Cysto-Urethrocele	7		18	11	2	4	6	2			50
Rectocele		14	27	10	5	16	14	12			98
Hemorrhoidectomy	48	52	51	46	38	35	26	39			335
Endocervicectomy	3	6	7	2		3		2			23
Amputation of cervix	14	9	3	8	7	5	3	4			53
Dührssen's incision	12	15	12	16	14	25	26	12	11	8	151
Miscellaneous	5	3	9	19	10	60	20	37	14	24	201
Total operations	946	942	1,125	1,069	1,115	1,291	1,730	1,534	1,226	1,339	12,317

TABLE V. COMPLICATIONS FOLLOWING DELIVERIES AND REPAIRS*

	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945	TOTAL
Fever of undetermined origin	2	11	2	4	15	18	16	20	2	10	100
Bronchitis	3	1			1		1				6
Pleurisy	1		1		1						3
Pneumonia	2	1		3		2	1			1	9
Retention of urine	4		1					1			6
Phlebitis	1				4	1		2			8
Thrombophlebitis		1		6	1	4	5	1	1	4	23
Perineal separation	6					2	1	1			10
Cystitis	12	8	13	10	10	12	18	16	15	19	133
Cystopyelitis	2	6	1	4	1	5	6	4	3	3	35
Shock	4		1								5
Transfusion reaction	6		1	1	1	3		1			13
Retained secundines		8	2			1		4	2	5	22
Atelectasis		1	1		1	2	3	2	4	3	17
Wound infection		1		1	2	2			3	2	11
Endometritis			4	14	10	17	16	6	2	3	40
Pelvic infection			1	1			2	1	4		9
Parotitis						1	1				2
Gastroenteritis			1				1				2
Inverted uterus									2		2
Postpartum hemorrhage			1				1		4	9	15
Total	43	38	30	44	47	70	71	60	42	59	504

*Cesareans omitted.

Duration of Hospitalization.—In earlier years, most of the patients left the hospital by the fourteenth to the sixteenth day. This was later cut to about twelve days. During the last few years, when hospital facilities have been so strained, the time has been greatly reduced, and most of the mothers now leave the hospital on the fifth day, as is customary in other hospitals in which puerperal operations are not performed. So far, we have not found that there is any injurious effect on the mothers in thus shortening their stay in the hospital.

Discussion

Although repair of new lacerations of the cervix had been reported many years earlier^{27, 28} and had been widely practiced, the procedure had been largely abandoned in 1918, when I presented my first report on this subject.¹ I was not aware that this had been done previously when I began the practice of repairing old injuries during the puerperal period, and certainly the teachings of that time were all against it. As I have reported in another publication,¹² I later learned that Stuart and Hussey had described some work of this type in 1906 and 1916. DeLee told me that he had attempted such repairs in 1898, but later abandoned them.

During the period that my colleagues and I have been performing operations for new, old, and combined lacerations immediately after delivery, numerous authors have reported cases of this type, though most of them do not carry out the work on the extensive scale that we have done. The majority of the publications deal with repair of primary lacerations, though some include old lesions, particularly of the perineum.

In previous reports, I have mentioned the work of Polak,^{11, 15} Pride,^{11, 15, 31} Potter,^{11, 15, 19} Sellers and Sanders²⁴ and Bailey, Toombes, Reinberger, Titus, Rongy, and Farrar, Friedlaender, Rothman, Kirshbaum, Bland, Boys, Williams, Holloway, Royston, Beardsley, Macdonald, Ristine, Wilson,¹¹ and Culbertson.¹⁵

Others who have reported some type of gynecoplastic operations include Emge,¹⁷ Kelly,¹⁸ McCarley,²¹ Emrich,²² Hanna,²³ Speidel,²⁵ Macfarlane and Howe,²⁶ Tracy,²⁷ Goff,²⁸ Christ,²⁹ Gayden and Plass,^{15, 30} Bernstein,³² and Guttman,³³ and Hirst.³⁴

The literature during the last few years has neglected this subject. Although some articles may have been overlooked because of obscure titles, a search of the *Index Medicus* failed to elicit any special reports of this work by other authors since 1937. It is discouraging to find, also, that numerous papers on progress in obstetrics³⁵⁻⁴⁰ omitted mention of these procedures in modern obstetric care. Since the results in our hands have been so eminently satisfactory, and the advantages so obvious, it is indeed difficult to see why so many remain indifferent to this type of puerperal care, or refuse to acquire the necessary skill to practice it.

Summary and Conclusions

A personal experience extending over thirty years in performing repair operations for new, old, or combined birth injuries immediately after the delivery is presented, along with additional statistical reports of puerperal gynecology as practiced in the obstetric department of Mt. Sinai Hospital from 1936 to 1946.

The importance of repair of cervical lacerations is stressed, and the salient features of the surgical technique are reviewed.

Our experience with thousands of operations performed immediately after delivery in a series of over 20,000 obstetric cases refutes all possible objections to these procedures. Although these operations require special training, skill, and care, they have proved successful in the hands of many different surgeons.

Advantages to the mother include improved general health, saving of time and money, prophylaxis against subsequent disabilities, and probable protection from cancer in later life.

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10515 CARNEGIE AVENUE.

CONSTRICTION RING DYSTOCIA*

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THE transverse extra or the intrauterine constriction ring complicating the first and second stage of labor still remains a serious problem. A review of 56 parturients, of which 54 were managed by qualified obstetricians, clearly demonstrates the necessity of further evaluating our management to improve the maternal and fetal mortality. The operative incidence in this series was 52, or 93 per cent, with two maternal deaths, or 3.5 per cent, and 18 fetal deaths, or 32 per cent. Failed vaginal operations occurred in 22, or 40 per cent, with a fetal mortality of 9, or 41 per cent. The types of constriction ring dystocia consist of: (1) the internal constriction ring and a potential prolonged first stage labor; (2) an external constriction ring complicating a potential prolonged first and second stage labor; (3) an internal constriction ring complicating the second stage labor. Our experience of this complication leads us to the conclusion that the management should be either one of ultraconservatism or a possible cesarean section. This should be based on the time the diagnosis is made during the first and second stage of labor.

We collected a series of 56 parturients from the Cook County Hospital, obstetric colleagues, and our private practices. Two were seen in consultation, while the balance were managed by qualified obstetricians.

The data of the series is as follows:

1. Mortality:
 - a. Gross maternal mortality of 2, or 3.5 per cent
 - b. Gross fetal mortality of 18, or 32 per cent
2. Parity:
 - a. Primiparas—27, or 48 per cent
 - b. Multiparas—29, or 52 per cent
3. Diagnosis was made:
 - a. First stage in 36, or 64 per cent
 - b. Second stage in 20, or 36 per cent
4. Gross operative incidence in 52, or 93 per cent
 - a. Fetal mortality of 16, or 30 per cent
5. Failed vaginal operations in 22, or 40 per cent
 - a. Fetal mortality of 9, or 41 per cent
6. Dührssen's incisions and forceps operation in 4, or 0.7 per cent
 - a. Fetal mortality of 1, or 25 per cent
 - b. Complications:
 1. Failed forceps in one which was followed by a craniotomy
 2. Shock in 3, one with severe sepsis
7. Diagnosis of the rings:
 - a. External in 21, or 38 per cent
 - b. Internal in 35, or 62 per cent

*Presented before the Central Association of Obstetricians and Gynecologists, Fourteenth Annual Meeting, Chicago, Ill., Sept. 19 to 21, 1946.

8. Location of the rings:

- a. Region of the "obstetric" internal os in 40, or 71 per cent
- b. Junction of the upper and lower uterine segment in 9, or 16 per cent
- c. In the upper uterine segment in 7, or 13 per cent

9. Delivery:

- a. Vaginal in 42, or 75 per cent
- b. Cesarean sections in 14, or 25 per cent (one a Porro cesarean section)
 1. First stage in 12, or 88 per cent
 - a. Maternal mortality 1, or 8 per cent
 - b. Fetal mortality, 0
 2. Second stage in 2, or 14 per cent (one a Porro cesarean section)
 - a. Maternal mortality, 0
 - b. Fetal mortality, 0

Diagnosis.—The cardinal criteria of the diagnosis of the complicating constriction ring of the first and second stage of labor remain the same as those given by the senior author in 1935,¹ except for the added importance of the transverse extrauterine constriction ring. They will be briefly reviewed. The diagnosis is speculative or absolute. The speculative diagnosis is a prolonged first stage, irregular uterine contractions, prolonged and intermittent periods of cervical dilatation, and the arrest of the presenting part in the second stage of labor.

The absolute diagnosis is the intrauterine palpation of a constriction ring, the state of the cervix and lower pole of the uterus, and a transverse extrauterine constriction ring. The signs and symptoms are as follows:

1. The uterine contractions vary in frequency, intensity, and duration. They may be of such a severe colicky nature as to cause the parturient to hold her abdomen with her hands with each contraction. Phillips² has called attention to these colicky uterine contractions in which the pain persists to and beyond the cessation of the contraction.
2. The station of the fetal head is stationary during the second stage.
3. The fetal head is loose in the pelvic cavity during uterine contraction which is pathognomonic.
4. The laxity of the cervix during the height of a uterine contraction. This is characteristic in that the cervix and the lower pole of the uterus are flaccid during the height of a uterine contraction. The external os does not contract or is not taut as it is during a normal uterine contraction, and is dilatable. When the cervical dilatation reaches 5 to 7 cm., the whole hand can easily be passed into the uterine cavity. This laxity is pathognomonic.

Mechanical dystocia (cephalopelvic disproportion, malposition, malpresentation, and pelvic and uterine neoplasm) should be ruled out during the prenatal supervision and shortly after the onset of labor for the management of a complicating constriction ring. This dystocia is not an active nor a predisposing factor.

The types of constriction ring dystocia may be stated as follows:

Type 1.—Internal constriction ring and a potential prolonged first stage labor. After eighteen hours of labor, the character of the uterine contractions and cervical dilatation (usually arrested for some hours) will indicate a prolonged first stage. The speculative diagnosis is a constriction ring dystocia. The absolute diagnosis is made by a sterile vaginal examination. The cardinal signs of the cervix and lower pole of the uterus is diagnostic.

Type 2.—External constriction ring and a potential prolonged first and second stage labor. The early appearance of a transverse extrauterine depres-

sion, furrow, or ring of the uterus at various levels, seen or palpated on the anterior abdominal wall is significant. During cesarean section we have seen and palpated these rings and found them to correspond with an internal ring at the same site. We have 14, or 67 per cent, parturients who had these rings early in labor from thirty-six to eighty-eight hours when operative procedures were undertaken to terminate the labor. This external depression or furrow (we refer to it as a ring) is diagnostic of an internal constriction ring which in our opinion is pathognomonic.

Type 3.—Internal constriction ring complicating the second stage of labor. The usual procedure in a forceps operation is palpation of the cervix for the dilatation, application of the blades to the fetal head, and traction. In a version operation, the usual procedure is to palpate the cervix for the dilatation and the upward displacement of the fetal head out of the pelvic cavity, and to grasp one or two feet and complete the turning of the child. When these procedures fail, an intrauterine examination is made to determine the cause of the difficulty. If a ring is in the region of the fetal neck, the examining hand can usually reach it without much displacement of the fetal head and with slight danger of prolapse of the cord, but when the ring is much higher the fetal head must be displaced out of the pelvic cavity with great danger of prolapse of the cord. When the ring is in the region of the fetal neck, it is from 6 to 10 cm. from the external os.

Treatment

The senior author in 1935 advocated a conservative management of the constriction ring dystocia of the first and second stage of labor which was based on his experience of 21 parturients and 350 parturients collected from the literature. A brief summary of his series will be presented: (1) gross maternal mortality of 54, or 15 per cent; (2) gross fetal mortality of 172, or 46 per cent; (3) external constriction rings of 24, or 9 per cent; (4) operative interference in 366, or 99 per cent; (5) failed vaginal operations in 154, or 42 per cent, of which 96, or 70 per cent, were failed forceps operations, with a maternal mortality of 26, or 27 per cent, and a fetal mortality of 27, or 33 per cent; (6) cesarean sections of 87, or 23 per cent, with a maternal mortality of 29, or 33 per cent, and a fetal mortality of 27, or 31 per cent. The experience gained from the above series and the present one has led us to adopt the management of first, ultraconservatism, and second, cesarean section which is based on the time the diagnosis of the constriction ring is made (Table I).

Conservative Management.—The basic principle involved is the maintenance of the parturient's mental and physical condition, and the prevention of maternal exhaustion during prolonged first and second stages of labor. It begins after eighteen hours of the first stage when the diagnosis is made of a potential prolonged first stage. The medical regime of maternal exhaustion is calculated for each twenty-four hours of labor. The urine is tested for acetone every twelve hours. A negative acetone test indicates that the parturient is being properly fed to prevent inanition and dehydration. The diet, liquid or soft, should consist of 3,000 calories of food rich in carbohydrates, and at least 2,000 c.c. of water for each twenty-four hours. This is best given in four-hour periods after an eight-hour period of consciousness which is used for feedings. Intermittent periods of sedation should be given to bring about the four-hour periods of rest or sleep. This regime is continued until the second stage is reached when the conditions present will determine the indication for delivery.

The ultraconservative management of constriction ring dystocia is to await the second stage until the ring has relaxed. This is determined by a further descent of the presenting part from its previous station. This will prevent hasty operative interference and failed operations in the second stage (Table II).

TABLE I. COMPARISON OF THE TWO SERIES

	1935	1946
Total parturients	371	56
Gross maternal mortality	54, or 15%	2, or 3.5%
Gross fetal mortality	172, or 46%	18, or 32%
Operative interferences	366, or 99%	52, or 93%
First stage interferences	81, or 25%	24, or 43%
1. Maternal mortality	10, or 13%	1, or 4%
2. Fetal mortality	44, or 56%	9, or 37%
External constriction rings	24, or 9%	24, or 38%
Failed vaginal operations	154, or 42%	22, or 40%
1. Maternal mortality	48, or 31%	0
2. Fetal mortality	123, or 80%	9, or 41%
Failed forceps operations	96, or 70%	13, or 59%
1. Maternal mortality	26, or 27%	0
2. Fetal mortality	66, or 69%	2, or 16%
Cesarean sections	87, or 23%	14, or 25%
1. Maternal mortality	29, or 33%	1, or 7%
2. Fetal mortality	27, or 31%	0
Version, and version and extraction	142, or 38%	4, or 7%
1. Maternal mortality	26, or 18%	0
2. Fetal mortality	81, or 57%	3, or 75%

TABLE II. FAILED VAGINAL OPERATIONS IN 22, OR 40 PER CENT. FETAL MORTALITY OF 9, OR 41 PER CENT

FAILED VAGINAL OPERATIONS	FINAL METHOD OF DELIVERY										FETAL MORTALITY
	NO.	PER CENT	FORCEPS	VERSION	EXTRACTION	SECTION	DÜHRSEN AND FORCEPS	CRANIOTOMY	DELAYED FORCEPS	DELAYED SPONTANEOUS	
Forceps	13	59		1		1			9		2
Version	3	14	2	1							3
Forceps and version	1	4.5				Porro					0
Dührssen and forceps	1	4.5						1			1
Extraction*	2	9			2						2
Craniotomy	1	4.5						1			1
Bag	1					1					0

*Breeches.

The management will be described under each type of constriction ring.

Type 1.—Management of an internal constriction ring and a potential prolonged first stage of labor. When the first stage is unduly prolonged, we speculate that the underlying cause is a constriction ring. After eighteen hours of labor, a sterile vaginal examination is made to determine the presence of the cardinal criteria of a constriction ring. If the diagnosis is a constriction ring, the management resolves itself to either the ultraconservative, or a possible cesarean section. The signs disclosed by the vaginal examination lead us to speculate on the probable duration of the labor. If we prognosticate that the labor will be unduly prolonged, the cesarean section may be elected, after a further functional test of labor of not more than ten hours to carry out this indication. There is no doubt that we erred in some instances, but we have learned from experience that in some cases that had labored forty or more hours, we wished in the retrospect that we had been more radical.

In this series we have 16, or 29 per cent, who were treated by a partial conservative management with one maternal death, or 9 per cent, and five fetal deaths, or 31 per cent. We note in this type vaginal operative interference in the first stage of 9, or 56 per cent, with a fetal mortality of 4, or 44 per cent,

while the second stage parturients were treated by the ultraconservative management in 7, or 44 per cent, with a fetal mortality of 1, or 14 per cent.

This type will be summarized:

Maternal death: A para ii, in labor fourteen hours when seen by the senior author in consultation, ten hours after being admitted to the hospital. The parturient was in good condition, but she was apprehensive. The fetal heart tones were 140 and good quality. The cervical lips protruded from the vulva, and were succulent. The hand was easily passed into the uterine cavity to find a mento left transverse position at station minus 3, and a rigid ring around the head and above the pelvic inlet. The distance from the constriction ring to the external os was about 16 cm. Diagnosis was mento left transverse position and constriction ring dystocia. A number of vaginal and intrauterine examinations were made before she had been seen. A conservative management was suggested and followed. The parturient was seen twenty-six hours later, and the above findings were still present, but she showed the effects of the labor. The fetal heart tones were still 140 and good quality. A Porro cesarean section was performed. A live child was delivered. After the supracervical hysterectomy was done, it was seen that venous blood was oozing from the anterior wall of the cervical stump. This venous hemorrhage was controlled with difficulty after blood loss of approximately 800 c.c. Blood plasma was started in the operating room, and whole blood was to be given when the patient reached her room. She left the operating room with a blood pressure of 110/70, pulse of 90 and good quality, and appeared to be in good postoperative condition. Shortly after reaching her room the parturient became irrational, so that it was impossible to transfuse her with the whole blood. She became dyspneic and cyanotic, and died within two hours after leaving the operating room. The cause of death appeared to be due to secondary hemorrhage from the cervical stump and shock.

Summary of the management of this type:

1. First stage. Cesarean section followed by maternal death (as above).
2. Ultraconservative management in eight with one fetal death.
3. First stage. Manual dilatation and forceps:
 - a. Successful with mother in shock and child alive.
 - b. Failed, which was followed by ultraconservatism with good results to mother and child.
4. First stage. Version and extraction in two with two fetal deaths.
5. First stage. Nine centimeters fetal distress, Scanzoni midforceps with fetal death.
6. First stage. Dührssen's incisions and forceps in two.
 - a. Mother in shock and child alive.
 - b. Failed operation followed by ultraconservative management and a fetal death.

Type 2.—External constriction ring and a prolonged first and second stage labor. The senior author in his series of 1935 found 24, or 9 per cent, external constriction rings complicating the first and second stage, and did not appreciate its diagnostic importance. In recent years we have found that this ring is frequently present and persists with prolonged labors. In this series we have eight instances of prolonged first and second stage labors in which the ring persisted, which were managed by cesarean section. We have learned that the degree of the spasmodic contraction and the persistence of the external constriction ring, signs of the cervix and the lower pole of the uterus, and the character of the uterine contractions indicate a speculative duration of a labor. In an external constriction ring with a prolonged first stage, we determine the man-

agement after eighteen hours of labor. With or without a sterile vaginal examination we will treat the patient conservatively, and after about ten hours more decide the management of either the ultraconservative or cesarean section. We believe that cesarean section is hazardous late in the first or in the second stage of prolonged labors. We note in this series we have eight cesarean sections which were performed after a labor of thirty-six to eighty-eight hours with good results. We have performed three cesareans after a labor of sixteen to twenty-four hours with good results. This may appear radical, but our experience with prolonged labors has demonstrated that the abdominal operation should be performed early, when the conditions are favorable, rather than late when the conditions are not favorable.

In this series we have 21 or 38 per cent external constriction rings present early in labor. The maternal mortality was one, or 5 per cent, and the fetal mortality was 3, or 14 per cent. Cesarean sections were performed in 12 parturients after a labor of thirty-six to eighty-eight hours with no maternal or fetal mortality. Vaginal delivery was done in nine parturients with a fetal mortality of 4, or 44 per cent. This type will be summarized to indicate the conditions and indications.

Summary of the management of this type:

1. Ring present when the second stage was reached. A difficult midforceps with the death of mother and child during the extraction.
2. Cesarean sections in 12 (hours of labor, one group of 36, 55, 56, 60, 48, 88 and 54: second group of 18, 20, 22 and 24 hours) with good results to mother and child.
3. Ultraconservative management in five parturients with a fetal mortality of one.
4. First stage, 9 cm., difficult version with the delivery of a live child; rupture of the uterus with the placenta in the abdominal cavity which was followed by a supracervical hysterectomy.
5. Dührssen's incisions and forceps in one with a live child; mother in severe shock and sepsis who recovered.
6. Conservative management to the second stage with the ring present. Failed low forceps on account of the ring around the neck. Some hours later a craniotomy was done.

Type 3.—Internal constriction ring complicating the second stage of labor. When an operative procedure is contemplated in the second stage after a prolonged first stage, a persistent station of the presenting part and the character of the uterine contractions should be speculative of a constriction ring dystocia, while an external constriction ring persisting is an absolute diagnosis of this dystocia. At this stage the cervical lips are retracted to or above the widest diameter of the presenting part. In the routine application of most forceps operations the absolute signs of a complicating ring are easily missed. Therefore, when the second stage is reached, the forceps or version operation is a trial procedure. When difficulty arises in an operative procedure, an intrauterine diagnosis is made to account for the apparent failure of the operation. Excessive traction should be avoided in a forceps operation when resistance is met in attempting to pull the fetal head out of the pelvis. When the diagnosis of a constriction ring is made, the ultraconservative management is instituted until the ring relaxes. This is recognized by the presenting part descending to a lower station. This is a presumptive sign that the ring has relaxed, but it may appear again during the operative procedure.

In this series we have 19, or 34 per cent, parturients who reached the second stage with no maternal mortality, and a fetal mortality of 8, or 42 per cent.

Failed operations occurred in 16 or 84 per cent, with a fetal mortality of 5, or 31 per cent. The ultraconservative management was followed in 12, or 63 per cent, and a fetal mortality of 4, or 33 per cent.

Summary of this type:

1. Failed forceps followed by a low cervical cesarean section.
2. Failed forceps operation followed by a Porro cesarean section on account of a prolonged labor and potential uterine infection.
3. A failed Dührssen's incisions and forceps in the first stage followed by craniotomy in the second stage.
4. Two failed breech extractions caused by a ring around the hips which, after relaxation of the rings, were followed by extraction with two stillborn infants.
5. Vertex, with a difficult forceps delivery caused by the constriction of the external os around the fetal neck. The child was stillborn.
6. Vertexes, eight, failed forceps operation caused by rings about the fetal neck. Ultraconservative management was followed in five to thirteen hours with good results.
7. Vertex, a difficult midforceps caused by a ring around the neck. Traction continued with the delivery of a stillborn infant.
8. Vertex, child died early in the first stage. In second stage a failed craniotomy occurred. Conservative management for six hours and stillborn infant delivered by cranioclast.
9. Vertex, failed forceps occurred. Adrenalin given, ring relaxed, and the forceps operation completed with good results.
10. Vertex, failed forceps occurred, and during the operation the cord prolapsed. Traction continued with the delivery of a stillborn infant.
11. Vertex, failed forceps occurred. The ring was around the neck. Adrenalin was given and the ring relaxed. A version and extraction was accomplished with a stillborn infant.

Discussion

Since Smellie in 1730³ described an internal constriction ring as a "navel string," 22 different terminologies have been applied to this complication of labor. The various current names are the ring of Bandl, contraction of the ring of Bandl, contraction ring dystocia of White,⁴ retraction ring dystocia of Pride,⁵ simply contraction or retraction ring, uterine contraction rings, and constriction ring of Rudolph.¹ Rudolph maintains that the ring occurs at various levels of the parturient uterus, i.e., in the upper uterine segment, junction of the upper and lower uterine segments, at the "obstetric" internal os, ring of Muller, or the true internal os of Schroeder,⁶ and the external os. Be as it may, the fact remains that it is becoming an established clinical entity by whatever name the complicating ring is designated. This clinical entity is as yet not well established in the diagnosis and management which necessitates our interest.

A review of this series demonstrates that the high operative incident, failed vaginal operations, fetal mortality, and the potential maternal mortality demands a careful consideration of the management of constriction ring dystocia. A comparison with the senior author's series of 1935 again demonstrates that our present series need to be evaluated.

The appreciation of the diagnostic significance of the external constriction ring in 21, or 38 per cent, parturients in this series has been the outstanding clinical sign to aid us in the management of this complication. Its early presence in labor, and its persistence in labor have indicated to us a potential prolonged labor, and its presence contraindicates vaginal operative procedures. We recognize that the prolonged first stage of labor is still a trying one in its management. It is well known that the ultraconservative management of a protracted labor invites a fetal mortality of about 10 per cent, and a slight danger to the parturient.

Some of the vaginal operative procedures in this series will be described in order to condemn them: (1) four Dührssen's incisions and forceps with one fetal death, one failed procedure which was followed by craniotomy, and resulting shock in all parturients after the delivery, and one parturient with a severe sepsis; (2) two manual dilatation of the cervix and forceps with one fetal death, one failed and then treated by the ultraconservative management with good results, and one parturient had mild shock after the delivery of the stillborn infant; (3) version, or version and extraction, four with three fetal deaths and one version and extraction with nine centimeters cervical dilatation with a live child delivered, but rupture of the uterus which was followed by a supracervical hysterectomy with good results to the parturient. These procedures appear to be relics of *accouchement forcé*.

The maternal deaths will be discussed: (1) The parturient seen by the senior author is unique in that he has not found nor seen a similar instance of the protrusion of a marked passively congested cervix and the lower pole of the uterus from the constriction ring. It was forty hours from the onset of labor when the Porro cesarean section was decided upon and performed. This death is left open for discussion. (2) A death from a midforceps operation when the external constriction ring was present. The parturient was in labor forty hours when the second stage was reached. The ring was present when the forceps operation was begun. After great difficulty in descent of the presenting part, an intrauterine examination was made which disclosed a constriction ring around the fetal neck. The traction was continued with a stillborn infant delivered, and the death of the mother as the infant was delivering. We believe that this parturient should have been managed by the ultraconservative management, or, if the child was dead or in a poor condition, a craniotomy, providing the parturient was not in shock.

The ultraconservative management will be agreed upon for the prolonged first and second stage. The suggested cesarean section will bring up the question of its abuse. We still believe that the vaginal route is the safest for the parturient, but constriction ring dystocia complicated by prolonged labor and the potential dangers of vaginal delivery must be seriously considered. The prolonged labor is still a problem in its physiology and management, but in cesarean section reports from various clinics, this operation is performed in instances of prolonged labor. When one reviews the statistics of constriction ring dystocia, we must appreciate the danger to the parturient with this complication. When one becomes conscious of this entity, and has learned to diag-

nose the complication early and to prognosticate the probable duration of the labor, then only does the cesarean section become an indication to be considered. We believe that after eighteen hours of the first stage, a vaginal and an intra-uterine examination for the cardinal criteria of constriction ring dystocia, or the presence of the external constriction ring will aid us in determining the indication for delivery. After waiting ten hours more we can decide definitely our management which is either ultraconservative or cesarean section for the safety of the parturient. The study of the series of 1935 and 1946 demonstrates that vaginal operative procedure must be carefully evaluated for constriction ring dystocia.

Conclusions

1. We have presented 56 parturients with a constriction ring dystocia.
2. The maternal mortality is 2, or 3.5 per cent, and a fetal mortality is 18, or 32 per cent.
3. The operative incident is 2, or 93 per cent, and the failed vaginal operations are 22, or 40 per cent.
4. The operations of Dührssen's incisions and forceps, manual dilatation of the cervix, and version and extraction are mentioned only to be condemned for constriction ring dystocia.
5. The ultraconservative management, and cesarean section when properly evaluated are the methods advocated by the authors.

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MINIMAL SPINAL ANESTHESIA IN VAGINAL DELIVERY*

An Analysis of 1,000 Consecutive Cases

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SPINAL anesthesia has certain distinct advantages over all other forms of regional anesthesia. If spinal anesthesia can be used in the obstetric patient with the same degree of safety as in the nonpregnant, it deserves a place in the obstetrician's armamentarium. All forms of regional anesthesia are accepted as the safest for the baby for the obvious reason that they minimize the danger of neonatal apnea.

Perineal block, parasacral, and sacral block, ideal as they are for many deliveries, do not give uterine anesthesia, and are difficult of administration to the uncooperative patient. Terminal caudal is a regional anesthesia that does give both uterine and perineal anesthesia, but caudal anesthesia presents inherent technical difficulties and, in addition, the time factor often restricts its use. After insertion of the needle into the caudal canal, one must wait ten minutes after injection of a test dose to make certain the needle has not perforated the dura. The anesthetic dose is then injected, and about fifteen minutes thereafter anesthesia is achieved. Most anesthetic casualties in the use of caudal block have been due to the inadvertent intrathecal injection of the necessarily large quantity of drug used. The generally accepted initial test dose implies this ever constant danger.

Numerous reports on the use of spinal anesthesia in obstetrics have appeared since Pitkin and McCormack's¹ report in 1928. Recent examples are papers by Parmley and Adriani,² and Weaver, Adamson, and Johnson.³

Spinal anesthesia in obstetrics has been in disfavor because of fear of blood pressure fall and shock, the danger of uterine atony followed by hemorrhage, and the danger of intrathecal infection and/or toxic reaction and neurological sequelae. The latter danger, namely, infection and/or toxic reaction, is not limited to the obstetric patient and occurs rarely indeed, as shown by the widespread use and proved safety of spinal anesthesia in the various surgical specialties.

As obstetricians, it was our belief that if a small dose were used, and if it were specifically placed, satisfactory anesthesia, both uterine and perineal, could be achieved without impairment of uterine motor activity and without sufficient vascular relaxation to permit blood pressure fall and shock. Gratifying results initially so encouraged us that we proceeded with this study to acquire a series large enough to permit certain significant clinical conclusions as to its effect on the conduct of labor and on morbidity and mortality, both fetal and maternal.

*Presented at the Fourteenth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Chicago, Ill., Sept. 19 to 21, 1946.

In order that the study might be of statistical value, routine admissions to the obstetric floor for vaginal delivery were given this method of anesthesia, with few exceptions. Elective versions were excepted because of the absence of adequate uterine relaxation. A few cases of frank breech were excepted where we did not choose to lose the "bearing down reflex" and then have to do a Pinard maneuver on one or both legs. Multiparas previously delivered without episiotomy were excepted in most instances. All patients were carefully questioned for history of disorders that would, in themselves, be contraindications to the giving of a spinal anesthesia. Disclosure at physical examination of any disorder of the spinal column or central nervous system was also considered a contraindication.

When the method was first undertaken, there was a necessary trial of dosage. As much as 30 mg. and as little as 15 mg. of metycaine were employed. After determining 22.5 mg. (1.5 c.c. of 1.5 per cent solution) to be the minimal practicable amount, we did not vary from this dose. This series includes 1,000 consecutive cases, with 1,008 deliveries, there being eight sets of twins. No cases having larger or smaller dosages are included in this report. These 1,000 patients all received 1.5 c.c. of a 1.5 per cent solution of metycaine in Ringer's solution, specifically 22.5 mg. Our definition of "minimal dose spinal anesthesia" in obstetrics implies the intrathecal administration of the smallest amount of an anesthetic agent specifically placed which will obliterate uterine and perineal pain in delivery.

In "minimal dose spinal" one is using one-twentieth of the caudal dose, and there is little uncertainty as to its destination upon injection. The injection requires only a very few minutes and anesthesia follows almost immediately.

Method

In this initial series the injection was made when the patient was ready for delivery, with few exceptions. In primiparas the cervix was completely dilated, and in most instances the head on the perineum; exceptions to the latter were instances wherein descent had ceased for a long enough time to warrant operative interference. Many multiparas were intentionally given their injections before complete dilatation. Anesthesia lasts about sixty to ninety minutes. One can anticipate completion of dilatation within that period of time in many instances of rapidly progressing labor and easily allow for delivery and episiotomy closure. Occasionally, rectal examinations were misinterpreted, and primiparas were given the injection before complete dilatation. In most of these instances also, dilatation was completed before the anesthesia "wore off." An occasional patient was given a second injection. Usually the injection was made with the patient on the delivery table; occasionally it was given in the labor room. With "minimal spinal," one does not sacrifice the patient's ability to cooperate in getting on and off the delivery table. She can usually move her legs, although there may be some adductor weakness. A blood pressure cuff is applied, and the Bell type stethoscope secured over the antecubital space. Long tubing permits placing the "Aneroid" and stethoscope headpiece by the patient's shoulder. This permits taking frequent readings without having to remove the arm from the fastened position at the patient's side. The left lateral position is generally employed; occasionally obese patients are placed in the sitting position. The skin

is prepared with soap, ether, and tincture of merthiolate. After draping, the first lumbar interspace is found. This level is chosen advisedly as being anatomically and physiologically correct because pain fibers from the uterus enter the spinal canal at the level of the eleventh and twelfth thoracic nerves. It is our intention to block them as close as possible to their point of entry into the spinal canal rather than depend upon large dosage and dispersion of the anesthetic agent to reach this level.

Metycaine 1.5 per cent in Ringer's solution is employed. After infiltration of the skin and subcutaneous tissues, using a 2 c.c. syringe of the same solution, a No. 22-gauge short beveled needle is inserted into the spinal canal. This small needle is used, hoping thereby to reduce to a minimum the subsequent trauma leakage of cerebrospinal fluid. A No. 20-gauge needle is also on the sterile tray and is used when the operator is unable to introduce the fine caliber needle into the spinal canal. After withdrawal of the stylette, and at the first appearance of a crystal clear "bead" at the needle's hub, 1.5 c.c. (22.5 mg.) of metycaine is injected from a 5 c.c. syringe. The injection is made slowly, between uterine contractions, thereby minimizing dispersion. The patient is promptly turned on her back, and the head of the delivery table raised one foot, about 20 degrees. After ten minutes, the table is returned to the horizontal.

A 1.5 per cent solution of metycaine is very slightly hyperbaric, and tends to seek a lower level. Within a few minutes, the sensory fibers of the second, third, and fourth sacral nerves are also anesthetized. These carry pain sensation from the cervix and lower birth canal. With this technique, anesthesia usually reaches a level between the umbilicus and the xyphoid. There is no obliteration of uterine motor activity. This function is thought to be controlled by fibers derived from the sixth thoracic segment. As previously stated, the patient can usually move her thighs, legs, feet, and toes. Immediately after the injection, the thighs are placed in stirrups, and preparations made for delivery in the usual manner. After the injection, the operator scrubs for ten minutes, and anesthesia is complete in fifteen minutes. The blood pressure is taken before the injection, and fifteen minutes and thirty minutes thereafter. An oxygen administration apparatus and the usual stimulants needed to combat vascular collapse are constantly kept in readiness.

Episiotomy followed by elective outlet forceps was practiced, but spontaneous delivery was encouraged when easy prompt outcome was anticipated. Many patients will bear down when told to do so, and, although the mechanism giving them the natural urge to push is obliterated, there is no paralysis of the abdominal muscles.

Of the 1,000 cases, there were 652 primiparas (65.20 per cent) and 348 multiparas (34.80 per cent). Of the total, 224, or 22.40 per cent, delivered spontaneously; 776, or 77.60 per cent, were operative deliveries. The operative incidence was 88.96 per cent in the primiparas and 56.32 per cent in the multiparas, as shown in Table I.

TABLE I. DELIVERY METHOD

	PRIMIPARAS		MULTIPARAS	
Spontaneous	72	11.04%	152	43.68%
Operative	580	88.86%	196	56.32%
Total	652	100.00%	348	100.00%

Operative procedures employed are shown in Table II.

Results

Anesthetic results were tabulated, listing uterine and perineal anesthesia separately. Each was evaluated on the basis of 1, 2, 3, or 4+. A 4+ was considered perfect anesthesia.

TABLE II. OPERATIVE PROCEDURES

	PRIMIPARAS	MULTIPARAS
Low forceps	545	187
Midforceps	22	6
Aftercoming head forceps	12	2
Internal version	2	1
Total	581	196

Interpretation of anesthetic results:

- 1+ Very slight anesthesia effect
- 2+ Unsatisfactory anesthesia (often requiring supplemental anesthesia)
- 3+ Mild discomfort
- 4+ Complete anesthesia

A 2+ result (either uterine or perineal effect) was considered unsatisfactory, and in these cases supplemental anesthesia was often necessary to complete delivery or episiotomy closure. A few cases, completed without supplemental anesthesia, were listed as failures because of the magnitude of the patient's complaints, namely, painful uterine contractions or perineal pain on delivery of the baby.

A perineal anesthesia failure (2+ or less) occurred in 53 cases (5.3 per cent), of which 13 were complete failures (1.30 per cent) (Table III). Of the 53 cases, 51, or 5.10 per cent, of the total 1,000 cases required some form of supplemental anesthesia. Twenty-five, or 2.5 per cent, required supplemental ether anesthesia for delivery and 24, or 2.4 per cent, were given pudendal block. One was given nitrous oxide inhalation, and one given intravenous sodium pentothal, as shown in Table IV.

TABLE III. PERINEAL ANESTHESIA FAILURES

Partial	40	4.00%
Complete	13	1.30%
Total	53	5.30%

TABLE IV. SUPPLEMENTAL ANESTHESIA

Ether inhalation	25	2.50%
Perineal block	24	2.40%
Nitrous oxide inhalation	1	0.1 %
Intravenous sodium pentothal	1	0.1 %
Total	51	5.1 %

In this series of 1,000 cases there were three instances of complete failure to relieve discomfort from uterine contractions (0.3 per cent). There were 31, or 3.1 per cent, who had only partial relief of uterine pain (Table V). On a rare occasion, a patient reported discomfort referred to the lower abdomen when forceps traction was applied. This same type of discomfort was occasionally noted when an occiput posterior was being rotated to the anterior position.

As previously stated, blood pressures were taken before injection, and fifteen minutes and thirty minutes thereafter. The average drop in pressure

TABLE V. UTERINE ANESTHESIA FAILURES

Partial failure	31	3.10%
Complete failure	3	0.3 %
Total	34	3.4 %

in the entire series was 14 mg. Hg systolic, and 7 mm. Hg diastolic. There were no instances of shock in the entire series. Also, there were no instances of nausea attributable to the injection, as is so frequently seen following spinal anesthesia when larger doses are used. Many patients have no perceptible fall in either systolic or diastolic pressure. The greatest fall in pressure occurred in one patient whose blood pressure of 92/62 before injection suddenly dropped to 68/25, but at no time did she show any clinical symptoms of shock. She was promptly given ephedrine sulfate ($\frac{3}{8}$ grain) intramuscularly and her pressure returned to its former level without incident.

Pulse changes in the entire series were checked carefully before and after injection. The physiologic bradycardia that normally follows delivery is apparently unaffected by an intrathecal anesthetic agent.

Although we have not been fortunate enough to determine blood loss accurately, a sincere effort was made in each instance to estimate it objectively. The average loss was very close to 100 c.c., definitely lower than blood loss encountered in cases where inhalation anesthesia was employed. A blood loss of over 500 c.c. was considered a postpartum hemorrhage. There were 11 instances so classified, or 1.10 per cent in 1,000 cases. Our impression is that minimal spinal anesthesia insures the same advantage in decreasing blood loss in the third stage of labor as has been quite generally accepted for caudal anesthesia. There was no instance of shock or sensitivity, as previously stated. All 11 postpartum hemorrhage cases responded without incident to the administration of intravenous ergotrate ($\frac{1}{320}$ grain) and blood replacement therapy, namely, plasma or whole blood. Uterine atony was not demonstrable clinically in any of these 11 instances.

Our criteria for morbidity was a temperature of 100.4° F. occurring on two or more days, not including the day of delivery. There were 43 such morbid patients, or 4.30 per cent, as shown in Table VI.

TABLE VI. COMPLICATIONS OF FEBRILE (MORBID) PATIENTS

Puerperal infection (endometritis, etc.)	20	2.00%
Urinary tract infection	10	1.00%
Mastitis	4	0.40%
Infection of perineum, etc.	4	0.40%
Dermatitis venenata (merthiolate sensitivity)	1	0.10%
Respiratory infection	2	0.20%
Infusion reaction	1	0.10%
Cause unknown	1	0.10%
Total	43	4.30%

Headache was the most annoying complication of the postpartum period. There was a total of 72 patients with this complaint (7.2 per cent). This includes all patients who required codeine grain $\frac{ss}{ss}$ on two or more occasions in an attempt to achieve relief. Inasmuch as headache is not uncommon after delivery, with labor, analgesia, anemia, fatigue, etc., playing a part, a postspinal headache was counted as such only in the absence of other obvious causes. Differentiation of causes was not possible in all cases, but there were nine instances (0.9 per cent) wherein there were other obvious causes for headache, such as toxemia, respiratory infection, etc. There then remained 63 instances, or a corrected incidence of 6.3 per cent, of the entire series wherein postpartum headaches seemed definitely postspinal in origin (Table VII). These varied in their duration, all having their origin in the first twenty-four to forty-eight hours, and lasting from one day to ten days.

Thirty of these 63 patients' charts revealed accurate data as to the day of subsidence of their postspinal headaches.

TABLE VII. PATIENTS WITH POSTPARTUM HEADACHE

Postspinal in origin	63	6.30%
Other causes established	9	0.90%
Total	72	7.20%

A review of Table VIII makes obvious the contention that this type of headache, when typical and definite, usually lasts through a week, and may persist longer. The more severe headaches usually persisted the longest. Our two cases of headache which lasted until the tenth postpartum day were the most severe in the entire thirty. No means, save repeated doses of codeine and the supine position, served to ameliorate this distress. In many of the mild cases of short duration we suspect that an element of suggestion plays a part. An occasional instance of lumbar backache or pain in the cervical region occurred. These were usually not associated with headache. In these latter instances, physiotherapy in the form of heat and massage offered quite prompt relief.

TABLE VIII. DURATION OF SPINAL HEADACHE

Subsided on the first day	0
Subsided on the second day	1
Subsided on the third day	4
Subsided on the fourth day	5
Subsided on the fifth day	8
Subsided on the sixth day	8
Subsided on the seventh day	2
Subsided on the eighth day	0
Subsided on the ninth day	0
Subsided on the tenth day	2
Total	30

With early ambulation (up on the second postpartum day), we believe the incidence of urinary retention has been kept to a minimum. Cases requiring catheterization two or more times in the postpartum period were classified as having urinary retention, and there were 15 cases encountered (1.5 per cent). Fourteen were primiparas and one was a multipara. Some obvious complication, such as traumatic delivery, infection, laceration, etc., was present to explain faulty bladder dynamics in all save three. In these three spinal anesthesia might have been a factor, but no proof exists as to the deleterious effect of the spinal in any of these cases.

There were no instances of infection at the site of injection, no meningeal infections, and no neurological sequelae.

There were 18 infant deaths, intrapartum or in the neonatal period (1.8 per cent), in this series. None of these deaths was attributable to the anesthesia, so the corrected fetal mortality was 0 per cent. Causes of death are listed in Table IX.

TABLE IX. UNCORRECTED INFANT MORTALITY

Prematurity	5
Congenital defect	5
Intrauterine death	2
Breech presentation (2nd twin)	1
Ablatio placenta	1
Placenta previa	1
Atelectasis	1
Pneumonia	1
Intracranial injury	1
Total	18 (1.80%)

Comment

Analysis of the results in these 1,000 vaginal deliveries conducted under minimal dose spinal anesthesia reveals no instance of the usually feared side effects of spinal anesthesia in the obstetric patient. The high incidence of outlet forceps delivery common to most regional anesthetic methods prevailed in this series also. The occurrence of postspinal headache in 6.3 per cent of the cases was the only undesirable subjective factor. The favorable effect on the baby plus the minimal trauma to the birth canal which can be achieved when such a high degree of perineal relaxation is attained suggests to us that this method of anesthesia for operative deliveries has many advantages over inhalation agents, and compares favorably with other regional anesthetic methods.

Summary

1. One thousand cases delivered under "minimal dose spinal anesthesia" are reported. There were 1,008 deliveries, there being eight sets of twins.

2. Metycaine, 22.5 mg. (1.5 c.c. of a 1.5 per cent solution), was found to be the minimal practical dose, and was used in every instance in this reported series.

3. Method of administration is described in detail.

4. Method of delivery and maternal morbidity is analyzed.

5. There were no instances of the usually feared side effects of spinal anesthesia in the obstetric patient.

6. "Minimal spinal anesthesia" in this series proved to be a safe and desirable anesthetic method for operative vaginal delivery, and the results indicate it deserves a place in the obstetrician's armamentarium for use in selected cases.

The opinions expressed herein are those of the writers and are not necessarily those of the Navy Department.

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THE MANAGEMENT OF DELIVERY FOLLOWING STILLBIRTH FROM PREVIOUS DYSTOCIA*

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THE obstetric patient who becomes pregnant after having lost her first baby from dystocia presents a problem that should receive the serious attention of the obstetrician or the physician who manifests an especial interest in obstetrics. The success which attends the second delivery of such patients may be considered a measure of the justification of specialization or of special interest in obstetrics. Women who have lost their first-born from dystocia have undergone a trying experience and a bitter disappointment. This distressing result obtains in only rare instances in the modern practice of obstetrics. It is almost imperative that a normal baby be delivered in future pregnancies. Women who comprise this small group of obstetric patients should have every assurance that a normal, living infant will be born at subsequent deliveries, but at the same time no unnecessary maternal risk should be involved.

Because a review of the literature for the twenty years from 1916 to 1936 failed to reveal a specific reference to cases of this interesting group, Mussey and one of us (A. B. H.)¹ felt a report of a series of cases was needed. That report was presented to this society ten years ago and covered experience at the Mayo Clinic with 33 cases of this obstetric complication during the decade immediately preceding 1936. We now wish to augment that report by presenting an additional 32 cases observed in the Section on Obstetrics of the Mayo Clinic in the decade that has intervened.

In the period covered by the initial report (of 33 cases) there were 3,953 deliveries, or an incidence of one stillbirth from dystocia for every 120 deliveries (0.8 per cent). During the past decade in which there were 32 cases, there were 7,265 deliveries, an incidence of one such case for every 227 deliveries (0.4 per cent). It is encouraging that the percentage incidence of these cases has been reduced by nearly 50 per cent in ten years. This fact probably represents improvement in obstetric practice in the community. The wider application and more intelligent use of prenatal care and such relatively recent improvements as roentgenographic pelvimetry may play a role.

The data gathered ten years ago is shown in Table I, together with the uncorrected fetal mortality rate of 4 per cent and a corrected fetal mortality rate of 2 per cent in 50 deliveries subsequent to fetal death from dystocia in the primary pregnancies.

Our data concerning experience with the same type of cases in the last ten and one-half years from Jan. 1, 1936, to July 1, 1946, is given in Table II.

*Read before the Fourteenth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Chicago, Ill., Sept. 19 to 21, 1946.

TABLE I. FETAL MORTALITY IN CASES ENCOUNTERED FROM 1926 TO 1935, INCLUSIVE*

	BABIES		FETAL MORTALITY, PER CENT
	LIVING	DEAD	
First delivery (at clinic or elsewhere)	0	33	100.0
Second delivery (elsewhere)	0	5	100.0
Next delivery (in five cases the third)	32	1	3.0
Subsequent deliveries	16	1	5.9
Total deliveries after first stillbirth	48	2	4.0
Corrected fetal mortality†		1	2.0†

*Table with emendations from Hunt, A. B., and Mussey, R. D.: *AM. J. OBST. & GYNEC.* 34: 310-315, 1937.

†On basis of one fetal death in 50 deliveries subsequent to stillbirth, the other infant dying of a congenital anomaly and urinary infection eighteen days after cesarean section.

TABLE II. FETAL MORTALITY IN SECOND SERIES (1936 TO JULY 1, 1946)*

	BABIES		FETAL MORTALITY, PER CENT
	LIVING	DEAD	
First delivery	0	32†	100.0
Subsequent deliveries	35	1	2.8

*Data on one patient was included in both series.

†One patient had two stillbirths before admission.

The initial fetal mortality rate by selection was 100 per cent. There was one fetal death in 36 subsequent deliveries. The mother who bore the dead infant lost her previous baby from a combination of severe toxemia and a delivery of accouchement forcé and forceps operation elsewhere. This patient was admitted to the hospital on the obstetric service with severe recurrent toxemia and a dead fetus in the uterus. If a correction may be allowed for this infant's death, there was no fetal mortality in the cases in the second series for the last ten and one-half years.

Histories of the Initial Pregnancies Involving Dystocia

Nine of the first series of 33 patients had been delivered as primigravidas at the clinic. Seven of the second series of 32 patients were delivered for the first time at the clinic. The babies of two of these patients were delivered through the pelvis at the clinic after attempts had been made elsewhere to deliver them. Difficulty in obtaining an accurate history in some cases precluded satisfactory analysis of the cause of the dystocia, although in most cases the cause could be determined rather readily. Actual bony dystocia seemed probable in 11 of the 32 cases encountered between 1936 and July 1, 1946. On the records of 21 of these 32 patients, notes clearly described difficult operative deliveries. These procedures were, in the order of their frequency, forceps delivery (often midforceps and high forceps operations), breech extraction, and version and extraction. Malpresentations of the fetus were important as evidenced by the incidence of eight breech presentations and one shoulder presentation. One patient lost two infants, and both deliveries were by breech extraction. Faulty uterine dynamics, as revealed by notes commenting on "uterine inertia" and "poor progress," were definite in seven cases, and probably the incidence of this important physiologic complication in labor is understated. There were several comments about "soft tissue dystocia" in the histories. There is circumstantial evidence that faulty timing of operative interference

often led to disastrous fetal results. Evidence suggested that there were several instances of premature operative intervention. Conversely, it seemed that perhaps some patients were allowed to labor too long for the good of the infant when conditions were favorable for a moderately easy operative delivery.

Deliveries After Previous Stillbirths

We may state as was done in the paper on this subject presented ten years ago: "The method of delivery to be employed for parous women whose babies have previously been born dead makes an interesting study. As term approaches, a selection must be made of those patients for whom a test of labor may be tried. The fact that a woman has lost a baby from dystocia does not indicate, per se, that elective cesarean section must be employed routinely in subsequent deliveries." The method of delivery used in the series of cases from 1936 to 1946 is correlated with the type of pelvis in Table III. No single criterion should

TABLE III. TYPE OF PELVIS CORRELATED WITH METHOD OF DELIVERY

TYPE OF PELVIS OR PERTINENT DATA	NUMBER	TYPE OF DELIVERY				DELIVERIES
		SPONTANEOUS	OUTLET FORCEPS	MID-FORCEPS	CESAREAN SECTION	
Gynecoid with adequate measurements	16	15	1	1	2	19
Anthropoid	2	2				2
Platypelloid	3	1			2	3
Platypelloid, small gynecoid	2				3	3
Gynecoid convergent	2		2			2
Gynecoid; android	1	1				1
Small gynecoid	2				2	2
Anthropoid with convergent canal	1				1	1
Anthropoid with marked midplane contraction	1				1	1
Previous fractured pelvis at delivery elsewhere	1				1	1
Two breech deliveries with stillbirth associated with recurrent toxemia	1				1	1
Total	32	19	3	1	13	36

decide the method of delivery. If the pelvis is adequate and there is a normal vertex presentation, the prospects for successful delivery through the pelvis are excellent. The physician who delivers the patient subsequent to stillbirth from dystocia has the tremendous advantage of the fact that the cervix has been dilated previously. Uterine inertia and so-called soft part dystocia are unlikely to reappear as a formidable complication.

Thirteen elective cesarean sections were done in the series of 32 cases encountered in the last ten and one-half years. In nine of these, definite pelvic contraction was the indication for such delivery. One of the remaining cesarean sections was done because the patient had sustained a fractured pelvis and soft tissue trauma at her primary delivery elsewhere which had required extensive orthopedic and plastic surgery. Another cesarean section was performed in a case in which two stillbirths previously had been associated with breech deliveries and recurrent toxemia. The other two cesarean sections in the presence of an adequate pelvis require comment. These two operations involved the same patient, a woman weighing more than 250 pounds (113.4 kg.). She was first seen in 1936 for emergency treatment because of failure of attempts to deliver the aftercoming head of a large fetus (which weighed 4,900 Gm.). Intrapartum sepsis existed from which recovery followed. She subsequently reappeared on two occasions with ruptured membranes and shoulder presentations

which had been promptly diagnosed by her physician elsewhere. These two babies weighed 5,850 and 4,840 Gm., respectively.

It is important to note that 23 of the 36 deliveries in this series were conducted without resort to abdominal delivery, and all were successful in fetal outcome but one. In this case a macerated fetus was due to severe recurrent toxemia and was delivered spontaneously through a normal gynecoid pelvis. Four patients were allowed a test of labor in the presence of some degree of pelvic contraction, and all were successful in the test. Except for three deliveries by outlet forceps, there was only one operative delivery among the 23 deliveries that were effected without resort to cesarean section. This was an instance of midforceps operation. About one-half of the patients in the group encountered from 1926 to 1935, inclusive, gave evidence on examination of bony disproportion requiring cesarean section. In only about one-third of the deliveries in the second group (1936 to 1946) was abdominal delivery required. This reduced number may indicate a better selection of patients with contracted pelvis for cesarean section.

There were no maternal deaths in our series (1936 to 1946), although there had been one maternal fatality from sepsis following cesarean section in the group of cases previously reported in 1936.

TABLE IV. FETAL MORTALITY IN COMBINED SERIES, JAN. 1, 1926, TO JULY 1, 1946

	BABIES		FETAL MORTALITY, PER CENT
	LIVING	DEAD	
From dystocia in first pregnancy	0	64	100.0
From dystocia in second pregnancy	0	6	100.0
Deliveries subsequent to stillbirth from dystocia	83	3*	3.5
Corrected fetal mortality		1†	1.2

*One infant died of anomaly on eighteenth postpartum day. There was one intrauterine death before admission from maternal toxemia.

†Mother of this infant was delivered of a surviving infant in 1946.

Data of the two series have been combined in Table IV. These are the total data from the twenty-year period concerning the outcome of deliveries following stillbirth from dystocia. The fetal mortality rate decreased from the initial 100 per cent to an uncorrected figure of 3.5 per cent. If a correction for the two deaths not related to delivery is made, the corrected fetal mortality rate is 1.2 per cent, or one death in 86 deliveries. The mother of the infant represented by this stillbirth was delivered of a living infant in 1946.

A total of 64 women is represented in the combined series. One woman was included in both series. Of these 64, two (only 3.1 per cent), do not have one or more normal living infants. One of these women lost her second infant as a result of severe recurrent toxemia which should probably interdict pregnancy in the future. The delivery of the second infant of the other patient was through the vagina and was normal, but the child died some months later. It was a Mongolian idiot and died of intercurrent disease. This woman is now pregnant and the prognosis for successful result is excellent.

Summary and Conclusions

The deliveries of 32 patients subsequent to stillbirth from dystocia in primary pregnancies are reviewed. These patients were seen at the clinic from Jan. 1, 1936, to July 1, 1946. A gross fetal mortality rate of one fetal death in 36 deliveries, or 2.8 per cent, was obtained. This infant was dead in the uterus because of a severe toxemia of the mother on her admission to the hospital. There

was no maternal mortality in this series. When these data are added to those reported ten years ago, it is found that 64 women had lost 71 babies from dystocia before this study was made. Subsequently they were delivered of 86 babies with three fetal deaths, a gross fetal mortality rate of 3.5 per cent. There was one maternal death early in the first series. The maternal mortality rate for subsequent deliveries was therefore slightly more than 1 per cent. Only two of the 64 women including the one that died are without normal living infants. One of these had normal delivery but lost her infant some months later from nonobstetric causes. She is now pregnant and the chance for a living baby is excellent.

The opportunity for *individual* prenatal care, examination, and study of the safest method of delivery is most valuable in the care of these patients. In these cases the conduct of the first delivery subsequent to the stillbirth from dystocia seemed to determine the outcome in later deliveries. Patients who were delivered successfully through the pelvis continued to have this type of delivery and those who had to submit to abdominal delivery again required this management.

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BLOOD CALCIUM: A NORMAL CURVE FOR PREGNANCY*

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NUMEROUS articles in the literature are evidence of the attention which has been given to the subject of calcium in pregnancy. However, relatively few of these articles deal directly with a series of determinations of blood calcium in pregnant women. Blair-Bell and Hick, in 1909, published the results of in vivo experiments performed on rabbit uteri to determine the response of uterine musculature to certain substances. Among other results, the response of the pregnant uterus to the intravenous injection of calcium salts was very marked, with the same type of uterine contraction as seen in labor. From their findings, they concluded that labor was not the result of any one reagent, but expressed the belief that calcium salts circulating in the blood, or excreted by the uterus, played the most important role in that connection; acting in conjunction, possibly, with certain other substances, such as pituitrin, secreted by the endocrine glands. Danforth and Ivy in 1939 published the results of a similar series of experiments in vivo performed on the uteri of dogs and rabbits in an effort to disprove or confirm these findings of Blair-Bell. An interesting part of their work was the use of sodium hexameta-phosphate intravenously to combine with calcium and prevent manifestation of its physiologic action. Their results clearly demonstrated that calcium played a vital role in the motor activity of the uterine muscle, even pituitrin and ergotrate having no effect in the absence of calcium. They suggested the possibility that physiologic variations in the reactivity of uterine muscle during labor might result from physiologic changes in the availability of calcium ions.

This article does little to confirm or disprove these interesting findings. It is simply a report of a series of cases studied at the University of Kansas Hospitals in an effort to establish a "normal" level of serum calcium for pregnant women. It was thought at the onset of the study that if calcium did play a vital role in the onset of labor, such information might be obtained if the serum calcium was correlated with the patient's progress throughout her pregnancy, labor, and the puerperium. Only primiparas were used in the series, and all determinations were made by the author after a practice period in which to become familiar with the method and eliminate, as far as possible, all sources of error. An attempt was made to follow each case throughout the course of her pregnancy, labor, and puerperium, with blood being drawn at monthly intervals during the pregnancy, once during labor, and once in the immediate puerperium, not more than fourteen days post partum. The samples, after being obtained, were kept at a cool temperature and, after the blood coagulated, the serum calcium was determined within a maximum period

*Presented before the Central Association of Obstetricians and Gynecologists, Fourteenth Annual Meeting, Chicago, Ill., Sept. 19 to 21, 1946.

of twenty-four hours. The method used was the Clark-Collip modification of the Kramer-Tisdall method. In this method, the serum calcium is precipitated as calcium oxalate to which normal sulfuric acid is added. The resulting oxalic acid is then titrated with 0.01 N potassium permanganate. The results with this method have an error of not more than 2 per cent. Every effort was made to observe the details of the method as carefully as possible to keep the results within this limit of error. Phosphorus determinations were also made on each sample of serum, but the results will be disregarded for the purposes of this paper, except to state that the calcium-phosphorus ratio was within normal limits for each sample. No effort was made to control the diet of the patients, other than the routine dietary instructions in our clinic, which include a quart of milk daily. The series includes a total of 185 cases, 119 of which might be called "completed cases," since they were followed throughout the entire course of their pregnancy, labor, and puerperium. However, nine of these cases developed toxemia and were eliminated from the study for that reason. The remaining 66 were "lost" for one reason or another after having at least one calcium determination made, but are used in the study since it was felt that their use would not affect the accuracy of the results. We were unable to obtain sufficient samples during the first trimester of pregnancy to produce an accurate curve for this period. In the "completed cases" a clinical record of the patient's labor was correlated with a record of the calcium determinations. Results were tabulated for each case, and the average of the total determinations for each particular period plotted on a graph as shown in Fig. 1. It is evident from inspection of the curve that there is a depression of the serum calcium during pregnancy which is most marked during the seventh and eighth months. The serum calcium apparently begins to decrease as early in pregnancy as the second or third month, which is what might be expected, since bone formation begins in the fetus as early as the seventh week. There is, of course, a question as to whether the serum calcium determination is an accurate index as to the actual amount of calcium in the body. Since we have no accurate, practical way of determining the amount of calcium in the body tissues, we satisfied ourselves with determinations of serum calcium. We also made no effort to differentiate between ionizable and nonionizable calcium in the blood. Despite the fact that the curve shows a definite depression during pregnancy, the difference between the lowest determination at eight months and the highest determination at two months is only 0.6 milligram. We feel that this difference is sufficiently small to make its clinical importance very doubtful. From our results, we also concluded that it would be impossible to correlate the individual case to this average curve, since the determinations for any particular case in the series did not necessarily show this depression.

For the purposes of comparison, the results obtained in this series were plotted on a graph with the results obtained by Mull and Bill in 1934, Plass and Bogert in 1923, and Widdows in 1924 (Fig. 2). Mull and Bill separated their curve according to the season of the year; January to May, and June to December, as shown above. The curve we obtained would appear to be

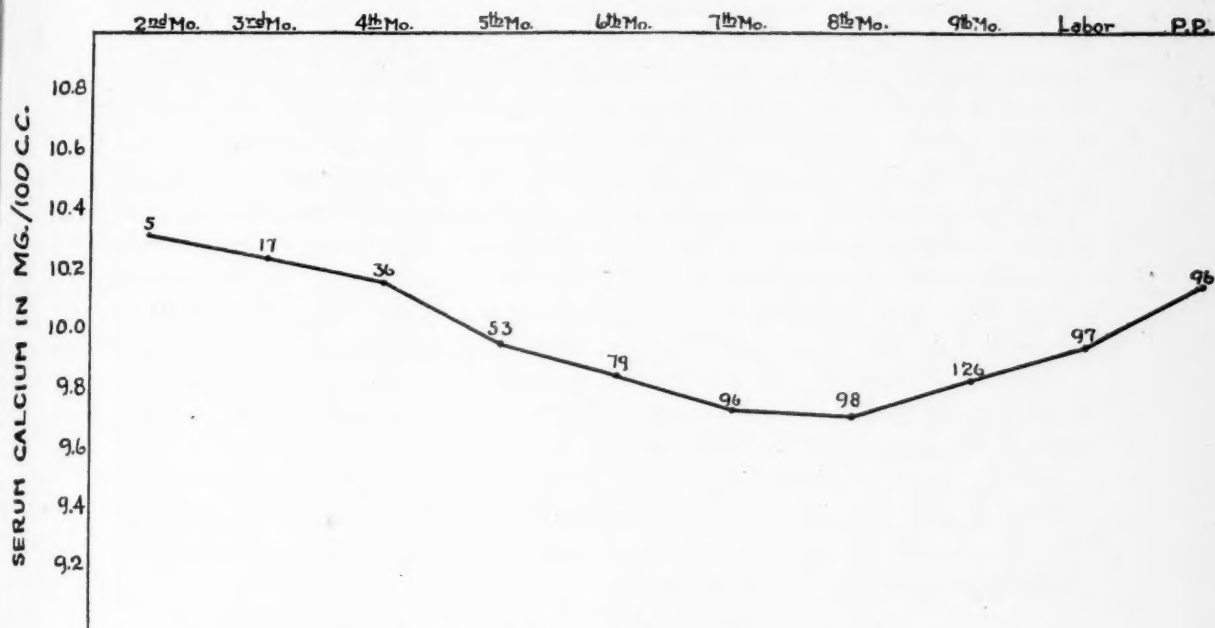


Fig. 1.—Serum calcium in pregnancy.

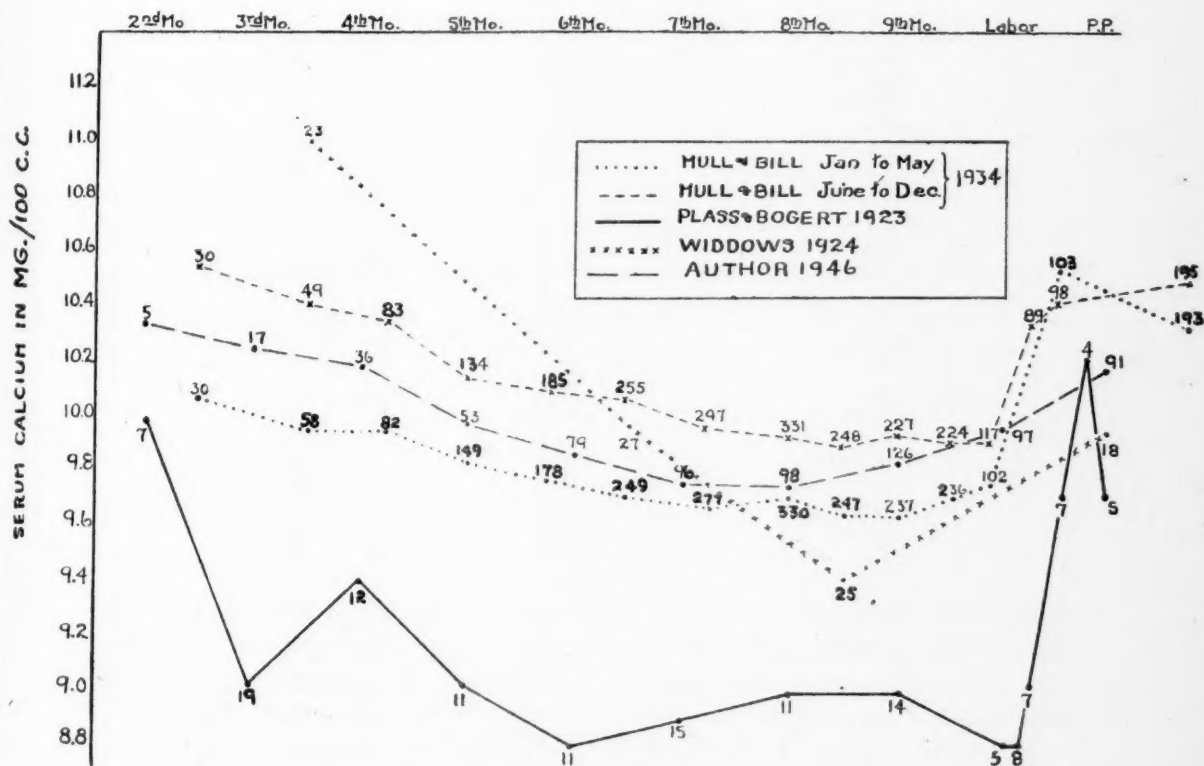


Fig. 2.—Serum calcium in pregnancy.

roughly an average between these two. Why the determinations obtained by Plass and Bogert should be so much lower than those in this series and that of Mull and Bill could be explained, perhaps, on the basis of the small number of determinations, since the same method of determination was used in all three series. It is interesting that, despite this fact, the general contour of all three curves is roughly similar, although the results of Mull and Bill and the present series most nearly correspond. Neither Mull and Bill nor Plass and Bogert ran determinations during labor, but from their results concluded that the serum calcium rose sharply after delivery. The results of the present series differ from those conclusions, since they indicate that this elevation occurs to a certain extent at the time of labor, but that this elevation is simply a continuation of the rise which began at the ninth month. The series of Widdows was somewhat incomplete, but very roughly corresponds to the findings in the other series, as shown in Fig. 2.

From the 110 "completed cases" in the present series, 20 cases having "short" labors, averaging seven hours and five minutes in length, were selected and the average of the serum calcium determinations for these 20 cases was determined with the following results:

MONTH	SERUM CALCIUM	DETERMINATIONS
Second	10.40	2
Third	10.03	5
Fourth	9.93	7
Fifth	9.72	11
Sixth	9.83	14
Seventh	9.66	15
Eighth	9.64	15
Ninth	9.78	19
Labor	9.96	20
Post partum	10.22	18

Similarly, 20 cases of "long" labor, averaging twenty-eight hours and thirty-five minutes in length, were selected and the following results obtained:

MONTH	SERUM CALCIUM	DETERMINATIONS
Second	9.91	1
Third	9.57	3
Fourth	9.95	9
Fifth	9.89	10
Sixth	9.78	14
Seventh	9.69	14
Eighth	9.83	18
Ninth	9.88	20
Labor	10.01	19
Post partum	10.35	20

These results are shown in Fig. 3. It was not felt that the differences in serum calcium determinations between the cases of "long" labor and "short" labor were sufficiently marked to be of any significance. As a matter of fact, from observation, it is evident that the two curves correspond rather closely.

Forty-six "plus" cases in which the serum calcium determinations ran consistently above the average curve had an average blood loss of 213 c.c. with an average labor of fifteen hours and fifty-seven minutes. Twenty-two "minus" cases with the serum calcium determinations consistently below the average

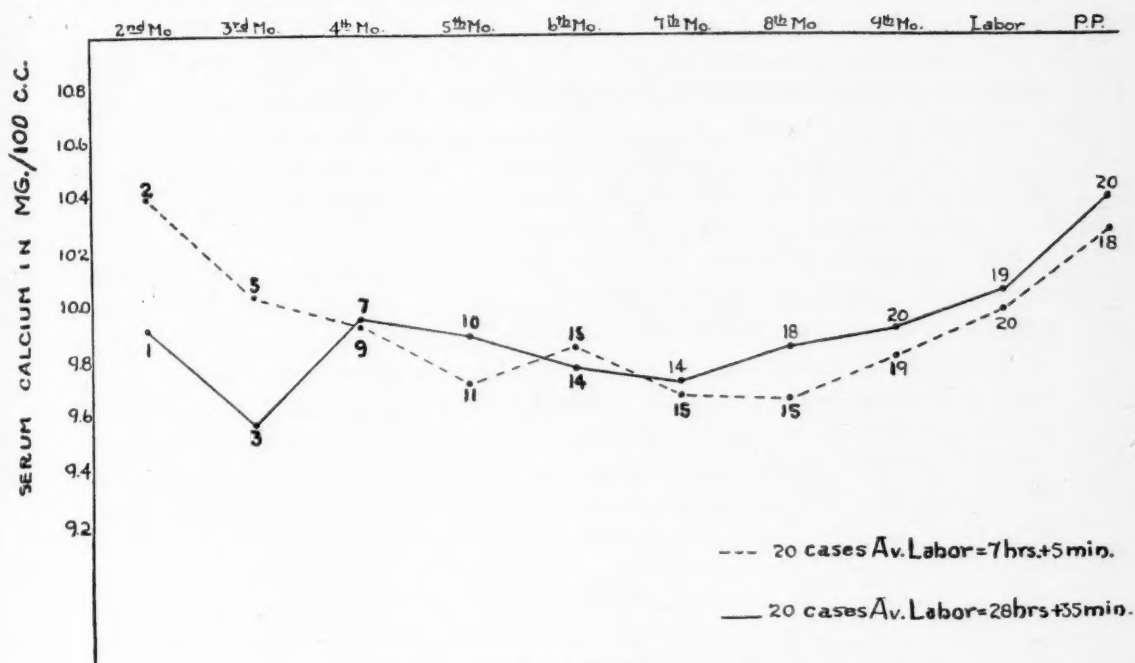


Fig. 3.—Serum calcium in pregnancy.

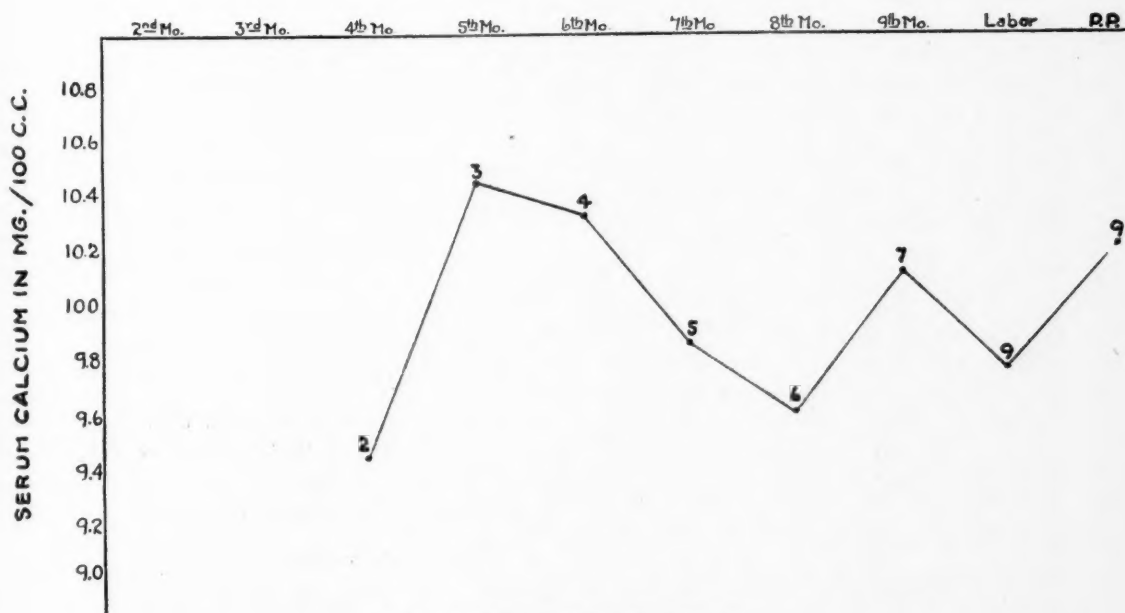


Fig. 4.—Serum calcium in toxemia.

curve had an average blood loss of 157 c.c. with an average labor of eighteen hours and twenty-seven minutes. These differences are not considered to be sufficiently great to be of any statistical value.

It has been previously mentioned that nine of the cases in the series developed toxemia. It is interesting that the curve of serum calcium determinations in these cases is very bizarre, not conforming at all to the average curve which has been presented. For the purposes of interest only, these results are shown in Fig. 4. It was felt that the number of determinations was too small to be of value in reaching any conclusions.

In conclusion, we have tried to demonstrate a "normal" curve of serum calcium in pregnancy, labor, and the immediate puerperium. The results indicate a depression of the serum calcium during pregnancy which begins to rise at the ninth month, the elevation continuing through the period of labor and almost reaching its early pregnancy level by the end of the immediate puerperium. This depression of the serum calcium is sufficiently small to make its clinical significance questionable. Results of the study would tend to indicate little relationship between the serum calcium level and the length of labor or amount of blood loss.

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EXPERIENCE WITH MIDPELVIC DYSTOCIA*

Preliminary Report

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CONTRACTION of the pelvic midplane sufficient to necessitate craniotomy can occur¹ in a patient with inlet and outlet measurements at the lower limit of normal. On the other hand, midpelvic dystocia is unlikely in patients with average or larger inlet and outlet measurements. It has been suggested^{2, 3} that midpelvic capacity is best evaluated by summation of the interspinous and posterior sagittal diameters. Guerriero, Arnell, and Irwin² believe that dystocia may be expected when the sum is 13.5 cm. or less, while Weinberg and Seadron³ favor 13.0 centimeters. There is need for collection and evaluation of accurate statistics on the pelvic midplane.

Patients

Serious interest in this subject at Parkland Hospital began a year ago and by June 1, 1946, the pelves of 140 patients were evaluated by a combination of radiographic mensuration⁴ and graphic portrayal.⁵ Because of film shortage, the first 102 patients included only those with varying degrees of contraction of one of the three essential pelvic planes. Later, some 12 women with unexplained stillbirth, or previously difficult forceps operations, were recalled and their pelves measured. Finally, in March, 1946, each primigravida and all multigravidas with previous difficulty were routinely submitted to radiographic mensuration and graphic pelvic portrayal. Preparation of this report began six weeks later and, therefore, only 26 of these women are included, although routine mensuration continues.

A résumé of the outcome of delivery in relation to the sum of the transverse and posterior sagittal midplane dimensions appears in Table I. In general, it will be noted that the frequency of necessary delivery operation and the rate of infant death decrease as this sum increases. It is, however, of considerable interest to note that in several instances vaginal delivery was accomplished successfully in spite of seemingly severe contraction. Pelvic contraction does not necessarily imply arrest of labor, and impressions gained solely from pelvic mensuration without consideration of size of the baby are often subject to error.

Of ten patients with midplane measurements totaling less than 13 centimeters (Groups 1, 2, and 3 of Table I), eight were delivered vaginally, three of them spontaneously.

In two patients (Group 1) the sum of the interspinous and posterior sagittal diameters was less than 12 centimeters. One was delivered spontaneously of a 2,912 Gm. infant. The other, with an unusually ample forepelvis, required midforceps operation, but produced a living 4,571 Gm. child!

*Presented before the Central Association of Obstetricians and Gynecologists, Fourteenth Annual Meeting, Chicago, Ill., Sept. 19 to 21, 1946.

TABLE I

GROUP*	SUM IS AND PS (CENTIMETERS)	PATIENTS NUMBER	DELIVERY			FETAL DEATH	
			SPON- TANEOUS	NECESSARY OPERATION			
				NUMBER	PER CENT	NUMBER	PER CENT
1	12.0	2	1	1	50.0	0	-
2	12.0-12.4	3	1	2	66.6	1	33.3
3	12.5-12.9	5	1	4	80.0	0	-
4	13.0-13.4	7	2	3	42.8	0	-
5	13.5-13.9	12	6	4	33.3	2	16.6
6	14.0-14.4	22	10	5	22.7	2	9.1
7	14.5-14.9	25	14	6	24.0	1	4.0
8	15.0-15.4	16	5	6	37.5	1	6.3
9	15.5	48	32	6	12.5	2	4.1

*Note that a definite "break" in the fetal death rate seems to occur between Groups 5 and 6. Also note that two patients in Group 1 gave birth to living children.

The fetal death in the second group of patients resulted from a craniotomy necessitated by insurmountable midplane disproportion after the head passed through the pelvic inlet. The other two infants were born spontaneously and by low forceps, respectively.

In the third group, the largest infant was born by cesarean section, the next largest by midforceps, two smaller by low forceps operation, and the smallest spontaneously.

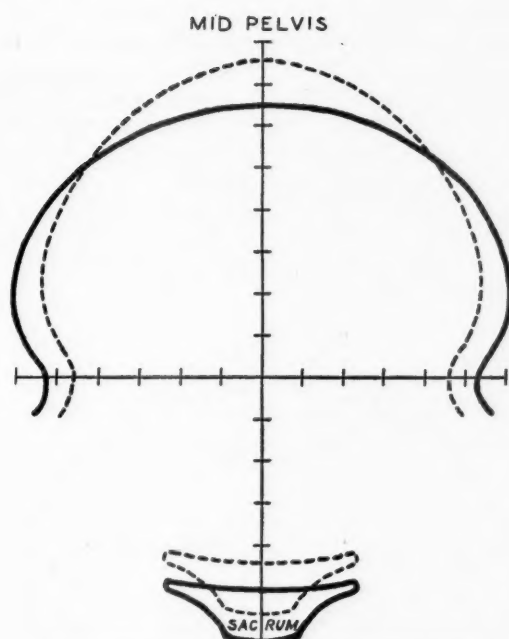
Prediction of the Course of Labor

In addition to analysis of the actual outcome of labor, the present report embodies a survey of the results of "prediction" of its course. In many instances, prediction was made after termination of labor, but may be accepted as reliable for the purposes of this report, since it was done without knowledge of the outcome.

Pelvic measurements of the patients in this series were graphically portrayed by means of the method recently described by Mengert and Eller.⁵ Fig. 1 illustrates the midplane of one of these patients (dotted lines) in immediate comparison with the normal prototype (solid lines). A plastic transparent model, Fig. 2, representing a small, medium, or large fetal head, was superimposed on the pelvic diagram. The relationship between the pelvic diagram and the plastic cutout permits understanding of the possibility of passage and of direction. In event of forceps delivery, superimposition of the fetal head model in various positions often indicated the mechanisms and rotations to be employed.

It was recently demonstrated³ that there is no constant relation between fetal weight and head diameter. However, the length or weight of the fetus is relatively of little concern from the standpoint of labor, in comparison to the size of the head. It is of considerable prognostic significance to be able to classify fetal heads roughly as small, medium or large. Abdominal palpation can supply this information. Also, the head can be measured from the films used for pelvic mensuration, provided the child is near term and the head is fixed.

Fig. 3 depicts the midplane, shown in Fig. 1, with the head model superimposed. Obstruction to the passage of a large fetal head can be readily visualized. It is equally apparent that a small head, represented on the model by the innermost diameter, will be able to traverse the midplane. Unfortunately for this patient, the fetal head was large, and difficult forceps rotation and extraction of a child lying in persistent occiput posterior, performed after two hours of complete cervical dilatation with the vertex well below the spines, re-



	Normal	Patient
Anteroposterior	11.5	11.9
Transverse	10.5	9.2
Posterior Sagittal	5.0	4.5

Fig. 1.—Diagram of a moderately contracted midplane.

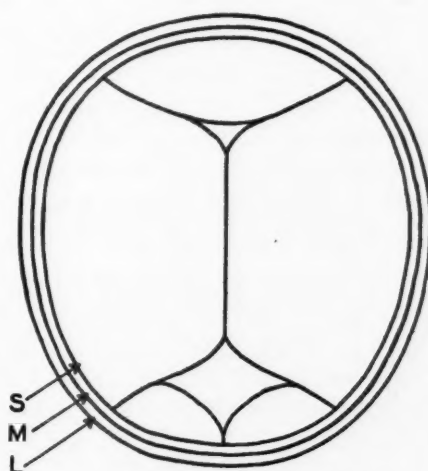


Fig. 2.—Transparent, plastic head model, with three head sizes: small, medium, and large.

sulted in a stillbirth. Autopsy revealed intracranial hemorrhage and dislocation of the second cervical vertebra.

"Prediction" was made in each of the 140 women in terms of "easy" or "difficult" vaginal delivery, or of necessity for cesarean section. "Easy vaginal delivery" was defined as spontaneous labor or elective low forceps operation, except when fetal death or injury from birth trauma resulted. "Difficult" was defined as vaginal operation necessitated by more than two hours of second stage with the cervix dilated and effaced.

A prediction of difficult delivery was made in twenty-five patients. Actually cesarean section was performed on five of them, thus eliminating them from proof of predictability. In seventeen of the remaining twenty patients, difficulty was experienced (Table II).

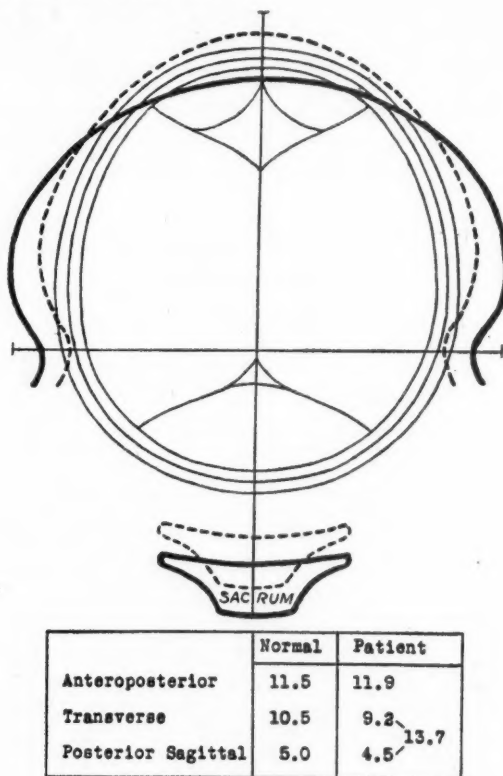


Fig. 3.—There is no room for the large size head in occiput posterior, in this midplane. The result is similar no matter whether the head is fitted in the fore or in the hind pelvis. On the other hand, the smallest size will go through.

Easy vaginal delivery was predicted for 115 patients, but 22 experienced some difficulty, as noted in Table III. In the group of 22 patients with incorrect prediction, there were three breech deliveries, two elective and unindicated forceps operations, and six patients with prolonged labor (more than thirty hours), thought to be due to uterine inertia rather than to bony dystocia.

Discussion

There is more to bony dystocia than pelvic mensuration. Fetal size, and moldability of the head, fetal attitude, and the force of uterine contraction must also be considered. Of these, fetal size alone is susceptible to quantitative

TABLE II. DYSTOCIA PREDICTED

17 Patients	
<i>Position:</i>	
Occipitoanterior	6
Persistent occipitoposterior	8
Persistent occipitotransverse	3
<i>Results:</i>	
Spontaneous delivery	1
(3¼ hours second stage, neonatal death from intracranial hemorrhage)	
Low forceps indicated	4
Midforceps	10
(1 stillborn, intracranial hemorrhage)	
Craniotomy	2
(Midpelvic arrest)	
Fetal loss	4 (23.5%)

TABLE III. DYSTOCIA NOT PREDICTED

22 Patients	
<i>Position:</i>	
Occipitoanterior	6
Persistent occipitoposterior	6
Persistent occipitotransverse	7
Breech	3
<i>Result:</i>	
Low forceps	5
Midforceps	14
Breech extraction	3
Fetal loss	5 (22.7%)

determination. Commonly, obstetricians are concerned with weight of the baby. On the other hand, the size of the head is more important from the standpoint of prognosis of the outcome of labor than the weight or length of the infant. Although fine gradations may not be feasible, radiographic fetal cephalometry permits classification as large, medium, or small.

In the great majority of patients, current methods of mensuration will reveal an obviously ample pelvis, with no reason to anticipate bony dystocia at any level. In the relatively small group with borderline inlet capacity, careful clinical observation of the degree of disproportion and descent, and of the forces and progress of labor, will generally allow an early determination of the procedure of choice. With outlet contraction, observation of progress is clinically unsound, and arbitrary decision must be made in advance.

Midplane contraction is somewhat analogous to outlet contraction, because observation of the progress of labor, with intent to interfere abdominally in case of arrest, is seldom feasible. Serious dystocia at the midplane is encountered more frequently than at the outlet, but midpelvic capacity is seldom evaluated prenatally. Therefore, universal effort directed at collection and evaluation of midplane dimensions and their effect on the course of labor is urgently needed.

Evaluation of midpelvic capacity of a small selected series of 140 patients showed that dystocia and fetal calamity were more common when the sum of the interspinous and posterior sagittal diameters was less than 14 centimeters. Thus, there were three fetal deaths in 29 such patients (10.3 per cent) as opposed to six among 111 patients with a sum of 14.0 or more centimeters (5.5 per

cent). On the other hand, term-sized children were born alive through the two smallest midplanes (12.0 centimeters) in the series.

When midpelvic capacity is reduced to dangerous limits, prediction of the outcome of labor, and foreknowledge of the mechanisms to be employed with forceps operation are greatly augmented by employment of transparent cephalic models superimposed upon a midplane diagram.

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AN EVALUATION OF THE CRITERIA OF DIAGNOSIS AND CURE OF GONORRHEA IN THE FEMALE*

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THE responsibility of making a diagnosis of gonorrhea or of ruling it out in an adult female is a serious one for any doctor because of the social, legal, and public health aspects. The gynecologist and the obstetrician are particularly concerned and should take the lead in establishing, at least for themselves, adequate criteria on which to make their decision. At present, in most communities, the diagnosis is a matter of clinical judgment supported by some type of laboratory evidence; the Public Health Service and the Armed Forces go further in their laboratory requirements, but few gynecologists are aware of the limitations of laboratory reports to support the statement that any individual woman either has or does not have gonorrhea, or that she is or is not cured of it.

Material

The material of this survey consists of 598 women from the Cincinnati Health Department clinic and from the Quarantine Hospital of the Municipal Workhouse, on whom over 6,100 smears and 3,200 cultures were reported. A good contact history was obtained on almost all of these cases by highly trained nursing personnel, and clinical observations on all of them were adequately made by one or more physicians with specialized training in venereology or gynecology.

The smears and cultures were done by the City of Cincinnati Health Department in its distinctly better than average laboratory. While specialized centers have reported culture accuracy greater than was found in this series, the value of this survey lies in the picture it gives of gonorrhea in the average large community with ordinary diagnostic facilities. It is the situation that faces most practicing physicians and the vast majority of clinics dealing with this problem. The number of cases is large enough to have statistical significance, and the purpose of the review is to stimulate the acceptance of criteria of diagnosis and cure that are actually adequate.

In trying to make a diagnosis of gonorrhea in the presence of clinical findings or a contact history or both, considerable reliance was formerly placed on a single smear. This also held true for ruling out gonorrhea in pregnancy, before marriage, for foodhandler examinations, employment examinations, institutional admissions, and for contacts. In this series of 598 women determined as being infected with gonorrhea, a single smear missed 59 per cent of the cases. On the other hand, a single culture missed only 38 per cent of them. The combination of a smear and a culture missed only 28 per cent, that is, only half as many as a single smear. When the suspects not already diagnosed were given two examinations at least twenty-four hours apart, the percentage of missed cases fell, on two smears, to 24 per cent, on two cultures, to 10 per cent, and on two of each, to 6 per cent. On three examinations the figures were, respectively:

*Presented before the Central Association of Obstetricians and Gynecologists, Fourteenth Annual Meeting, Chicago, Ill., Sept. 19 to 21, 1946.

6 per cent, 3 per cent, and 0.2 per cent. These figures demonstrated that only with three smears and three cultures could the diagnosis of gonorrhea be ruled out with any reasonable assurance.

The question of cure is even more difficult. Most recent literature on gonorrhea deals with the relative merits of one or another technique of administration of sulfonamides or penicillin. But a survey indicates a wide disparity in the criteria used for cure, varying from two negative cultures in six days to ten negative cultures in three months. In this particular series, only 431 of the women were treated by the clinic or the quarantine hospital, the rest either being sent to private physicians or other clinics, or else leaving town. Cures were effected by one or two courses of sulfathiazole or penicillin or one of each, in 401 women, that is, 93 per cent. The remainder required more treatment. There were four failures after four courses of penicillin. As it is not the purpose of this paper to compare techniques of cure, the discussion is limited to what constitutes a cure and how it affects the handling of the individual woman. More than one-fourth of the cases were in quarantine and incapable of being reinfected. While the possibility of reinfection of the others existed, it was minimal due to the careful contact histories obtained, and, where any doubt existed, the case was considered a reinfection. The difference between the two groups of figures was found to be insignificant, a phenomenon reported by many other authors, so that the 431 cases were considered in one series.

A single culture twenty-four hours after the completion of ten days' treatment with 2.0 Gm. of sulfathiazole or after the administration of 200,000 Oxford units of penicillin in four two-hourly doses of 50,000, missed 84 per cent of the failures to cure. A smear and a culture missed 65 per cent. A second culture forty-eight hours after treatment missed 72 per cent of the failures; the second smear and culture missed 37 per cent. Within ten days after treatment, a total of three cultures missed 24 per cent, and a combination of three smears and cultures missed 8 per cent of the failures to cure. Thus, by setting up any combination of smears and cultures as a criterion, the rate of cure will read almost any percentage.

That these figures are not usually high is borne out by the findings of Koch¹ and his co-workers in San Francisco. Dealing chiefly with males, they reported 71 per cent of failures missed by the first posttreatment culture and 62 per cent on the second. Blair,² at the Women's Federal Reformatory in West Virginia, confirms the observation with the remark: "In most cases (of cure failures) positive tests were obtained by the third check, although several were not found until the fifth or sixth specimens."

The importance of time among the criteria of cure cannot be overemphasized. Considering only the women in quarantine, incapable of being reinfected, the failures of treatment with sulfathiazole were first picked up as follows: three within the first two weeks after completion of treatment, seven in two to four weeks, and two cases after one month. With penicillin, while most of the failures were detected in the first fortnight, two cases merit brief description: Bernice M., treated with 200,000 units of penicillin on January 20, had three successive negative smears and cultures in the following two weeks. She was "cured" by the standards used there and at a great many other institutions. But just before release from jail on March 27, she had a positive smear culture. Catherine B. was treated on February 11 with penicillin and considered cured after three successive negative smears and cultures. But on May 20, just prior to release from confinement she had a positive culture. Thus the organisms, apparently destroyed by penicillin in these two women, became manifest two and three months respectively after pronouncement of cure and noninfectiousness by prevailing standards. Attention is invited to Koch's report

of 38 per cent of his failures in men after five or more weeks of negative observation. Thus, the glowing reports of cure in the literature must be slightly discounted unless the cures were confirmed over a period of months. The importance of this to the individual woman and her husband is obvious.

Discussion

In analyzing why smears or cultures in such a high percentage of cases fail to reveal the presence of the gonococcus, three factors come to mind. The first, in connection with putative cures, is the biologic one, and it is largely in the realm of theory. Questions may be asked, such as: Can sulfonamides or penicillin destroy only a certain percentage of organisms, or inhibit them, the remaining few lurking in the body to reproduce slowly and become detectable only after the passage of time? If so, then much work is needed to throw light on what the time factor is. Does the gonococcus exist in small numbers in secretions of the genital tract out of biologic contact with the blood stream and hence exempt from the action of sulfonamides or penicillin? If so, consideration must be given to adjuvant local treatment. In any case more knowledge is needed.

The second factor is the method used for taking the specimens. It was found that the percentage of false negatives dropped noticeably when the cervix was first wiped out thoroughly, and any tenacious mucus removed by winding on a thin swab. The swab for taking the specimen was inserted deep into the canal up to the internal os and pressed vigorously against the walls of the canal, while at the same time the jaws of the bivalve speculum were partially closed against the cervix so as to milk out cervical secretions. Better results were also noted just before, during, and immediately after menstruation.

The third factor is the laboratory procedure. Dealing for the moment only with false negative reports, the commonest laboratory error in examining smears is a failure to search long and thoroughly enough for the occasional Gram-negative intracellular diplococcus. It is a time-consuming process that few laboratories can afford, and for that reason a great many laboratory directors prefer to receive cultures for diagnosis.

The superiority of cultures over smears has been repeatedly proved but the wider use of cultures has been hampered by the technical difficulties of processing. The gonococcus is delicate, and numerous bacteriologic requirements must be met before reliance can be placed on negative reports. Actually, however, the difficulties are not formidable, and once a routine is established the use of cultures becomes quite easy for the doctor, the clinic personnel, and the laboratory. For private practice a messenger service to a laboratory within a few hours of procuring the specimen seems essential, but attention is invited to the preliminary work in North Carolina reported by Hirschberg,³ using a solid medium with which cultures may be sent by mail.

In this study the medium used was a chocolate agar (Difco bacto-proteose No. 3 and bacto-hemoglobin), which is in common use. That even greater accuracy may be obtained with other media is demonstrated by a recent work of Weller and Williams⁴ showing that a modified Peizer plasma-hemoglobin gave

40 per cent better results, and the Mueller-Hinton starch agar 27 per cent better results than did the Difco preparation. The actual technique followed was that of Carpenter⁵ with minor modifications. In the earlier days of the study, before numerous processing errors were noted and corrected, there were many false negatives not ascribable to the correctly performed culture method, but all cases are included in this series so that the advantage of cultures over smears does not reach the two to three figure reported in the literature.

In making a diagnosis of gonorrhea, the culture technique in this study, uncorrected, proved 1.7 times more accurate than the smear. In detecting failures of cure, however, the culture was not significantly more accurate. This suggests the importance of the biologic factor referred to above. Confirmation is found in comparing the results of smears and cultures taken at the same examination. Of these, false negative reports were given 742 times, of which both smear and culture were wrongly negative on 183 occasions, only the smear wrong 240 times, and only the culture wrong 136 times. In breaking down the ratio of false negative reports it was found that in diagnosis the culture was 1.5 times more accurate than the smear (292:193) whereas in the detection of treatment failures there was no significant difference (133:126).

Incalculable social harm can be done by the making of an erroneous diagnosis of gonorrhea, so that the question of false positive reports deserves attention. In this series of 9,300 tests there were only 56 false positive smears and eight false positive cultures. Of these, eight smears and one culture were from eight women who did not have gonorrhea; they represent pure laboratory errors. The remainder were in women who were treated, some with sulfonamides and some with penicillin, and there is a question of whether they represent laboratory errors or biologic peculiarities. All of these women had a long succession of negative smears and cultures following the false positive findings. The time elements were: in the first three days after penicillin treatment, 26 positive smears with negative cultures, and two positive cultures with negative smears; in from four to fourteen days, eight and three respectively; in the third week after treatment, 11 positive smears with negative cultures, and one in which both smear and culture were positive. In many clinics this case would have represented a treatment failure, but in the absence of clinical findings or contact history, and in the presence of seven subsequent negative smears and cultures without intervening treatment, the case was indubitably a laboratory error. False positive errors are due usually to the presence of other *Neisseria* such as: *catarrhalis*, *sicca*, *flava*, and *intracellularis*. These are indistinguishable by ordinary staining technique but may be differentiated from *Neisseria gonorrhoeae* by subculturing in certain sugars.

In this connection there may be mentioned briefly the results of a study, as yet incomplete, of 97 cases diagnosed as vulvovaginitis in children. A careful review of the records with particular reference to clinical findings and smears and cultures without treatment, or after extensive treatment, suggests that 45 of these were not gonorrheal, 23 were doubtful, and only 29 actually were due to the gonococcus. Of 821 smears, only 67 per cent gave correct results, but of 477 cultures, 97 per cent were correct. Of the false positive results, 89 per cent

were smears. It is probably safe to say that smears are not to be relied on for either a diagnosis or a criterion of cure, and that even cultures of these children require subculturing in the carbohydrates before designating the gonococcus as the offending organism.

Summary

1. This study involves over 6,100 smears and 3,200 cultures in the diagnosis of 598 cases of gonorrhea in the adult female, and the treatment of 431 of them.

2. A single smear missed 59 per cent and a single culture, 38 per cent of the infected cases, but three smears and three cultures missed only 0.2 per cent. As a criterion for cure, three smears and three cultures in the ten days after treatment missed 8 per cent of the treatment failures.

3. The culture proved 1.7 times as accurate as the smear for diagnosis but no more accurate than the smear for the detection of treatment failures.

4. False negative laboratory reports are due to (a) some biologic factor of which little is known, (b) the technique in taking specimens, and (c) laboratory errors. These, in the case of smears, are most commonly the result of insufficient study of the slide, and in the case of cultures are due to the delicacy of the organism and its need for special handling.

5. False positive results may be socially disastrous. They are found rarely with a properly performed culture.

6. In vulvovaginitis, of which 97 putative cases were studied, the smear proved of little value because of the high percentage of false positive reports. Cultures, including sugar differentiation, should be the sole method of diagnosis.

7. In adult females both smears and cultures should be used, as the accuracy of diagnosis is increased significantly. The smear offers an opportunity for a rapid report if it is positive. The culture technique presents some difficulty for other than institutional practice, but it is feasible under most circumstances.

8. Stricter and more uniform criteria for the diagnosis and determination of cure of gonorrhea in the adult female should be established by professional agreement. The minimum proposed to rule out gonorrhea is three smears and cultures, and to determine a cure, a succession of smears and cultures over a period of two months.

Appreciation is expressed to Dr. Carl A. Wilzbach, Health Commissioner of the City of Cincinnati, for permission to use the material surveyed and for many helpful suggestions; to Dr. A. H. Rodenburg, of the Cincinnati Health Department staff for advice with clinical problems, and to Mr. Otto P. Behrer, City of Cincinnati Bacteriologist, for help with laboratory problems.

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PENICILLIN AND ACUTE PUERPERAL MASTITIS*

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ACU TE mastitis is an aggravating complication of the puerperium. The rapid and specific action of penicillin, when used early in this infection, is dramatic. Neither local nor systemic sulfonamide therapy is satisfactory. The initial favorable results with penicillin have stimulated further investigation of this method of therapy and can be reported now.

Incidence of Puerperal Breast Infections.—It has long been recognized that acute puerperal mastitis is an institutional disease, but Fulton^{1, 2} recently re-emphasized this point. Apparently there is a geographical variation in the number of cases encountered. In this country the accepted figure is from 0.5 per cent to 2.0 per cent, and the incidence of this series of cases falls within that average. In England, Fulton found a breast abscess which either required incision and drainage or evacuated itself spontaneously in 16 per cent of patients delivered in the hospital, while 3.5 per cent of those delivered at home developed suppuration of the breast. In a later study of 250 patients, 25 per cent developed an abscess. Such an incidence is difficult to explain, especially when strenuous efforts were made during the study of the second series to reduce the frequency of the disease.

Penicillin and Breast Infection.—Early experimental investigation with penicillin demonstrated its value in soft tissue infections. This experience suggested its clinical trial in inflammatory diseases of the breast. Fraser³ treated 15 patients by aspiration and instillation of penicillin into the abscess cavity, resulting in resolution without drainage in only three cases. Hodgkinson and Nelson⁴ in 1945, and Power and Cravotta⁵ in 1946, reported excellent results using intramuscular penicillin during the cellulitis phase of the disease. Further clinical trial has justified these original claims.

Present Series of 73 Cases.—This report is based upon the experience of treating 73 infected breasts observed since 1942. The definition of puerperal breast infection used for this group was based upon well-established clinical facts. The history as obtained from each patient was essentially identical: sudden onset of pain in the breast, followed shortly by chills and hyperpyrexia. The average temperature upon admission was 101.6° F. although variations as high as 106° F. were encountered. The leucocyte count was as high as 31,000, averaging 15,600, with corresponding elevations in neutrophile percentage. Examination usually disclosed a mass in the breast underlying an area of erythema. Occasionally the involvement was diffuse. Simple congestive states were eliminated by the time of onset which averaged twenty-four days from the time of delivery. Only one patient experienced trouble as early as the twelfth postpartum day.

While the majority of infections developed in the postpartum period, seven of them cannot be considered true instances of puerperal mastitis. In the latter classification are two patients whose breast suppuration was neither related to pregnancy nor lactation. Prepartum breast infection developing in the eighth

*Presented before the Central Association of Obstetricians and Gynecologists, Fourteenth Annual Meeting, Chicago, Ill., Sept. 19 to 21, 1946.

and ninth months of gestation was encountered twice. Two infants, each one month of age, accounted for three more abscesses. Two of the abscesses evacuated themselves spontaneously, while one was incised. It is interesting that the infant with unilateral involvement was admitted with its mother who was also suffering from acute mastitis. Both were treated with intramuscular penicillin. While the mother's breast responded, the infant's failed to do so, and spontaneous evacuation of the pus occurred within twenty-four hours after admission.

In the puerperal mastitis group, 18 patients, when first seen, were suffering from abscess. Sixteen of the breasts required incision and drainage, while two cleared after aspiration. Forty-eight patients were treated with intramuscular penicillin during the cellulitis phase of the disease with complete resolution in each instance. This amazing response was reflected by the evident decrease in morbidity which averaged 6.1 hospital days. Recovery was complete. In contrast, the surgically treated group required 42.2 days from onset to complete healing.

Dosage.—Originally, treatment consisted of a total dosage of 840,000 Oxford units of penicillin. Twenty-five thousand Oxford units were given intramuscularly every three hours for seventy-two hours, and then 15,000 Oxford units every three hours for forty-eight hours. Symptomatically, all patients were well after sixty hours of treatment, but, because of the frequency of bacterial "persisters"¹⁰ in staphylococcal infections, it was felt wise to give the full five-day treatment. Penicillin blood levels taken one-half hour after administration averaged 0.371 Oxford units per milliliter. This was well above the optimum level of 0.156 required for staphylococcal infections.

Green, Burkhardt, and Hobby⁷ reported the presence of penicillin in 8 of 11 human milk samples. In contrast, Seeley and his group⁸ failed to identify penicillin in cows' milk after intravenous administration of 500,000 Oxford units, and concluded that the bovine mammary gland was not permeable to penicillin. In the present study, 10 normal patients, used as controls, were given, intramuscularly, 300,000 Oxford units of penicillin in oil and wax. Under as aseptic precautions as possible, milk was obtained both before and eight and one-half hours after administration of penicillin. A sample of blood was obtained at the time of collection of the last milk specimen. Cultures and bacterial counts were performed on the milk specimens while both blood and milk samples were assayed for penicillin.

The results are detailed in the tables, and it is obvious that penicillin did not materially influence either the contaminating organism or the bacterial count. No penicillin was identified in any of the milk specimens. However, we were technically unable, using a variety of methods, to identify traces of penicillin in milk. The penicillin level in the blood eight and one-half hours after its administration was consistent with the results of Romansky and Rittman.¹⁸ The beneficial effects from penicillin in the treatment of human puerperal breast infections are apparently due to the penicillin in the blood stream rather than that in the milk.

Nursing State.—In this series, breast infection was incident to weaning in 17 patients, while the remaining number were nursing their infants. When present, lactation was inhibited by the usual measures including the use of diethylstilbestrol in a total dosage of 40 milligrams. This plan was elected because of early experience with three patients in whom inhibition of lactation was not practiced. Each was treated with penicillin for a mild breast infection during the immediate postpartum period. The infection promptly cleared and they were encouraged to continue nursing their infants. About two weeks later each of the three patients developed acute mastitis in the contralateral

TABLE I. MILK SPECIMEN OBTAINED BEFORE ADMINISTRATION OF PENICILLIN

NUMBER	MILK CULTURE	BACTERIAL COUNT PER C.C.
1	<i>Staphylococcus</i>	
2	<i>Staph. aureus</i> , hemolytic	3,000
3	<i>Staph. albus</i> and <i>Staph. aureus</i>	1,840
4	<i>Staph. aureus</i>	20,600
5	<i>Staph. aureus</i>	4,600
6	<i>Staph. aureus</i> and <i>Staph. albus</i> (coag. pos.)	980
7	<i>Staph. aureus</i> (coag. pos.), nonhemo- lytic streptococcus	1,200
8	<i>Staph. aureus</i>	7,500
9	<i>Staph. aureus</i> (coag. pos.)	7,500
10	<i>Staph. aureus</i> (coag. pos.)	9,200

TABLE II. 300,000 OXFORD UNITS PENICILLIN IN OIL AND WAX GIVEN INTRAMUSCULARLY. SPECIMENS OBTAINED EIGHT AND ONE-HALF HOURS AFTER ADMINISTRATION

PENICILLIN BLOOD LEVEL	MILK CULTURE	BACTERIAL COUNT PER C.C.	PENICILLIN MILK LEVEL
.062	<i>Staphylococcus</i> and a few colonies of streptococcus		0
.030	<i>Staph. aureus</i> , hemolytic	2,000	0
.061	<i>Staph. aureus</i>	1,800	0
.062	<i>Staph. aureus</i>	9,400	0
.310	<i>Staph. aureus</i>	1,800	0
.248	<i>Staph. aureus</i> and <i>Staph. albus</i> (coag. pos.)	5,060	0
	Streptococcus, hemolytic		
.200	<i>Staph. aureus</i> (coag. pos.)	4,800	0
	Nonhemolytic streptococcus		
.128	<i>Staph. aureus</i>	4,000	0
.240	<i>Staph. aureus</i> (coag. pos.)		0
.240	<i>Staph. aureus</i> (coag. pos.)	20,000	0

breast. The opinion that lactation should be inhibited is strengthened by the knowledge that the concentration of penicillin attained in breast milk is insufficient to sterilize the milk. There has been no reactivation of infection since adopting this plan.

Breast Prophylaxis.—Proper breast hygiene is stressed as a measure of prophylaxis. Stander⁹ places the responsibility of the infection directly upon the attending physician or nurse, laying the cause to neglect.

Numerous bacteriologic studies have demonstrated that the usual puerperal breast abscess is caused by a coagulase-positive strain of staphylococcus. Routine culture from the throats of the newborn, the mother, and their attendants are commonly positive for *Staphylococcus aureus*. DeLee¹⁰ stressed for many years the frequency with which staphylococci could be cultured from breast milk. In a relatively recent study, Schlaeppli¹¹ found *Staphylococcus albus* and *Staphylococcus aureus* constant contaminants, with an occasional patient harboring a streptococcus. He further demonstrated a bacterial inhibiting substance in human milk which was later identified as lysozyme by Rosenthal and Lieberman.¹² Blatt and Kessler¹³ confirmed these observations. The immunologic implications of these studies as related to puerperal breast infections are suggestive.

Proper breast hygiene, therefore, must include control of such environmental factors as well as attention to the nipple. Miles and co-workers¹⁴ showed that the nasal carrier rate of the *Staphylococcus aureus* in England averaged 47.4 per cent. A recent editorial in *Lancet*¹⁵ suggested the use of penicillin as a spray or mist to the nose and throat of mothers and hospital attendants as a measure

of control. Knott and Blaikley¹⁶ have enforced this type of program for the past two years, and stated that the incidence of micrococcus carrier infections in the maternity ward was reduced 50 per cent by such spraying. Local penicillin to the nipples remains to be evaluated as an agent of merit. We have used penicillin ointment with some apparent benefit to cracked and fissured nipples, although the number of cases is too small to permit evaluation.

Suppurative Mastitis.—The distressing feature of a breast abscess is the prolonged morbidity, since the usual patient is under medical care for almost one and one-half months. In the present group of 18 cases of simple abscess, the time from onset to complete healing averaged 42.5 days. The tendency of the infected breast to develop secondary suppurative foci has long been recognized. Velpeau¹⁷ in 1853 reported as many as 52 separate abscesses in one breast. He stated that the duration of illness depended upon the individual duration of each purulent formation. Penicillin can be expected to prevent this complication, and its administration is advised for those patients requiring surgical drainage. This opinion is shared by Power and Cravotta.⁵ It has been the clinical impression in patients so treated that convalescence is shortened. Decrease in drainage, pain, and induration has been evident.

The limit of breast cellulitis is generally considered as being about forty-eight hours, and persistence of infection after that period of time usually results in suppuration. It has been our custom to give patients the benefit of a trial of penicillin therapy, regardless of the duration of symptoms, unless there was an area of softening indicating a localized abscess. Two patients who had evidence of infection for five and seven days, respectively, failed to show the expected response to the five-day plan of treatment. Aspiration on the fifth day yielded a small amount of pus from which was cultured *Staphylococcus aureus*. Because central softening of the mass could not be demonstrated, penicillin therapy was continued for five additional days with complete resolution. This type of case must be considered as borderline for penicillin therapy, and failure of the treatment can be expected in a certain number of instances due to errors in judgment.

Sulfatherapy.—The results obtained in this group of patients with sulfonamide therapy were disappointing. Five per cent sulfathiazole cream was used as a nipple dressing in many of these patients. It is apparent that it offered little protection. Before penicillin became available, 12 patients were treated during the cellulitis phase of the disease with various sulfonamides in apparently adequate dosage. Nine patients required incision and drainage of an abscess, giving a failure of 75 per cent. Four patients were admitted for penicillin treatment after having failed to respond to sulfadiazine. All promptly resolved when penicillin was given. One patient was admitted for incision and drainage of an appendiceal abscess. Six grams of sulfonamide were deposited into the abscess cavity, and sulfadiazine was continued orally, 1 Gm. every four hours. In the midst of this therapeutic program a breast infection developed on the seventh postoperative day. The more energetic action of penicillin appears to be required for this type of infection.

Disadvantages of Penicillin Therapy.—The main objections to penicillin therapy are required hospitalization, frequency of injections, and cost. Of the methods advocated for decreasing the frequency of injections, the oil and wax penicillin preparation of Romansky and Rittman¹⁸ appears the most practical. Four patients in the present group have been treated with this preparation. One injection of 300,000 Oxford units was administered every second day until three doses had been given. The response was as satisfactory as could be expected from the multiple three hourly injection method herein described. Hospitalization was not necessary, and the cost was not prohibitive.

Conclusions

1. Penicillin, if given sufficiently early, will prevent suppuration in acute staphylococcal puerperal mastitis.
2. Because penicillin is not secreted in the milk in sufficient amounts to control contaminating staphylococci, it is felt advisable to inhibit lactation to prevent reinfection of the breast.
3. Sulfonamide therapy is not recommended as a substitute for early penicillin therapy.

The bacteriologic work, including penicillin assays, was performed by Miss Edna Jackson of the Bacteriological Department, Division of Laboratories, Henry Ford Hospital, Detroit, Michigan.

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A 55-POUND SOLID UTERINE MYOMA*

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ON JAN. 3, 1888, Hill¹ successfully removed a 47-pound fibroid. On Dec. 16, 1902, Webster² surgically obtained an 87-pound cystic myoma with survival of the patient.

On July 30, 1906, Cullen³ successfully extirpated an 89-pound cystic myoma. Reporting the case eight months after operation, he stated that the 58-year-old patient "is in perfect health and is gaining rapidly in weight." He said that she had noticed the tumor for twenty years, and that she was delivered of a healthy baby about eighteen years prior to operation. Although suffering from the large abdominal tumor, she was able to do her work until three weeks before being referred to Cullen. Her chief inconvenience had been her inability to lie on her back in bed, "and sometimes when she would get stalled, it was necessary for her husband to turn her over quickly, otherwise, she would have suffocated." Upon making an incision over the most prominent part of the tumor with the patient in a sitting position and under ether anesthesia, an attempt to puncture it proved unsuccessful. Bleeding occurred, thereupon the incision was enlarged to the xiphoid process and the tumor removed in toto. Within eight hours after operation the temperature rose to 102.2° F. but dropped to 100° F. by evening. The highest pulse rate was 130. Postoperative vomiting is said to have been absent. The legs were bandaged on account of the edema. Catheterization was required only once. On the fourteenth day diarrhea caused considerable discomfort and "persisted off and on for a couple of weeks. At this time, however, the weather was excessively hot, and diarrhea was general throughout the hospital," he wrote. Twenty-three days after operation the patient weighed 80½ pounds, in comparison to the 174 pounds which she weighed upon admission. The pathologic description included, "the growth is, however, evidently made up of one large cystic state and numerous smaller ones together with the semisolid area." Kelly and Cullen,⁴ in their excellent book on uterine myomas, considered this case to be the largest authentic successful one on record.

In 1923, Farmer⁵ reported recovery after removal of a 35-pound tumor. The following year Marshall⁶ successfully removed a 47-pound myoma. On May 26, 1925, Stevens⁷ extirpated a uterine fibromyoma weighing 47 pounds, 5 ounces. The patient, aged 59 years, had five children, and had reached the menopause at 49 years "after some years of severe menorrhagia." She knew that she had had the tumor for twenty years. The operation was performed under chloroform anesthesia, using a block and tackle of which a photograph is shown in Stevens' article. The incision was about eighteen inches long and the "tumor was almost spherical in shape and contained a few small cystic cavities without other important degenerative changes." "The day after operation the respirations rose to forty per minute without any rise in temperature and without bronchitis or other lung complications." Other than this very rapid breathing

*Presented at the Fourteenth Annual Meeting of the Central Association of Obstetricians and Gynecologists in Chicago, Ill., Sept. 21, 1946.

for the first week, there was no cause for anxiety during convalescence according to the author, who reported the case five months after operation and stated "the patient is learning to walk again, and there seems to be every prospect that she will make a complete recovery."

In 1933, Greenhill⁸ reported a cystic fibroid weighing 47 pounds, and simulating an ovarian cyst which was removed at autopsy performed Oct. 24, 1928. He stated, "Because of the rarity of the occurrence of large uterine fibrocysts, the difficulty in making a correct clinical diagnosis, and the relatively large number of deaths which occur without operation due to disturbances in circulation, breathing, and cachexia, I am reporting this case." The patient was a 48-year-old Negro nulligravida, upon whom paracentesis has been performed about seventy-five times during the last year. Menses ceased four months prior to admittance to Cook County Hospital, and the patient had been free from menstrual disturbances. Her condition was so grave that operation could not be performed.

Report of a 55-Pound Myoma

Mrs. M. L. M., T-43-59162, born in New Orleans June 6, 1883, of Spanish parents, was admitted to the hospital on Aug. 15, 1942, complaining of "swelling of the stomach," inability to walk, orthopnea, marked weakness, etc. During the summer of 1925 she first noticed a mass "about the size of an orange" in the lower abdomen.

In 1932 the tumor had reached the umbilicus and a visit was made to the office of the mother's physician, who advised surgery. The patient declined as she "thought operation would mean death;" furthermore, she was free from pain and uterine bleeding. During the next ten years her health continued to be "good," and she performed all of her household duties, even though the tumor became larger and larger. However, in July, 1942, the mass had assumed such proportions that she was mechanically incapacitated. On Aug. 1, she became bedfast and complained of marked weakness. Upon being seen at home by one of us (H. T. B.), she bemoaned the fact that her abdomen was "bigger than the rest of the body," and she firmly believed that an early death was inevitable. She consented to be hospitalized.

Interrogation revealed that the menses began at the age of 11 years, occurred regularly and normally without pain every twenty-eight days, lasting five days, and finally disappeared at the age of 42 years. There were no known pregnancies. The tumor was first noticed shortly after the cessation of her last menstrual flow.

Review of systems revealed the following positive findings: loss of adipose tissue, progressive for four years; night sweats without known nocturnal fever; palpitation at times; dyspnea which had increased to the stage of orthopnea; dependent edema for "at least four or five months"; chronic constipation, partially relieved by mineral oil. The urinary index was not abnormal, nor were there any urinary symptoms.

Past history disclosed no previous hospitalizations or serious injuries. The family history revealed no evidence of neoplasia.

Upon admission to the hospital, the following data were obtained: temperature 100.6° F., pulse 100, respiration 30, weight 145 pounds, height 56 inches, circumference of abdomen 51¼ inches, and blood pressure 130/78. The patient had an abdominal enlargement to such a degree that she could not stand alone. Emaciation was marked. The skin of the abdomen and lower extremities was under great tension due to swelling. The mucous membranes were pale. The thorax was bilaterally symmetrical with an upward and outward displacement

of the lower ribs. The xiphoid process was displaced cephalad. Atrophy of the mammary glands was such that they hung as folds of skin. Moist râles were audible over the lung bases. The heart was displaced laterally. The peripheral arteries exhibited evidence of sclerosis.

An asymptomatic umbilical hernia was present. The superficial blood vessels were plainly visible. There was no evidence of free fluid in the abdomen.

The labia majora and minora showed evidences of atrophy. The vaginal introitus admitted the smallest Graves' speculum. Senile changes were present. The cervix uteri could not be palpated, as it had been drawn up by the pelvo-abdominal tumor. The hard nontender mass filled the pelvis and could not be

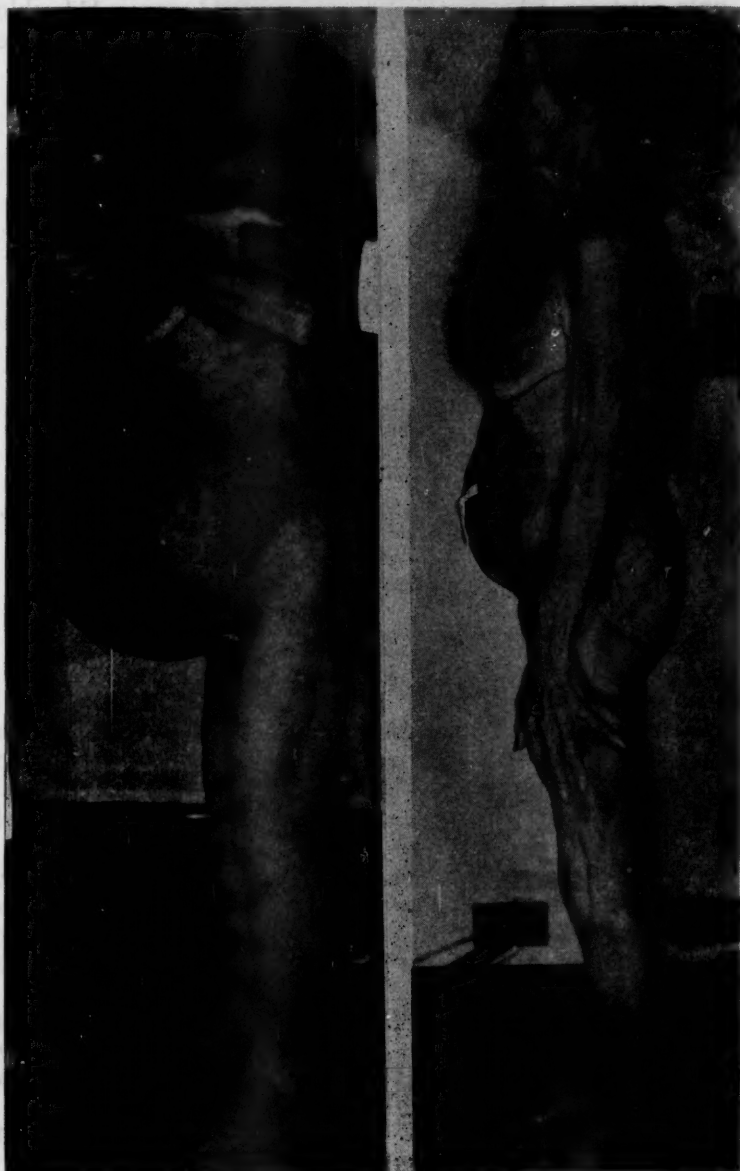


Fig. 1.—A, Aug. 21, 1942, patient too weak to stand alone. Weight, 145 pounds. B, One month postoperatively she weighed 70 pounds.

displaced. The uterus could not be outlined, nor were the ovaries palpable. External hemorrhoids were present. The mass encroached upon the anterior wall of the rectum.

On admission, the urine presented the following findings: alkaline, specific gravity 1.015, 2 plus indican, a trace of albumin, innumerable leucocytes, and many Gram-negative bacilli. Four days later there had been a marked decrease in the number of leucocytes present. On the day of admission the hemogram was: hemoglobin 55 per cent, erythrocytes 4,700,000, leucocytes 29,250, with 90 per cent polymorphonuclear neutrophils. Platelets, coagulation, bleeding, and blood sedimentation rates were essentially normal. On the second day after admission, urea nitrogen 8.9 mg. per 100 c.c. of blood, sugar 111, chlorides 976, and serum proteins 6.16 Gm. Blood Kline and Kolmer tests were negative.

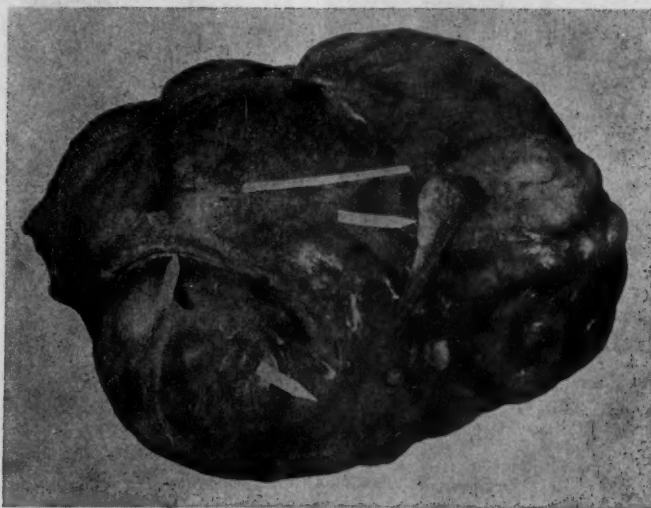


Fig. 2.—Tumor weighed 55 pounds. Note the six-inch rule.

A high caloric, vitamin rich diet was begun on admission. An indwelling urethral catheter was inserted, and sulfathiazole was given to combat urinary tract infection. The patient received blood transfusions and supplementary fluids in the form of 10 per cent dextrose in water. Mild laxatives and enemas were required. Seconal, morphine sulfate and scopolamine were given preoperatively.

Upon arrival of the patient in the operating room, with the urethral catheter in place, an infusion was begun through a No. 17 gauge needle. The skin was prepared with ether and tincture of merthiolate. A short infraumbilical incision was made under procaine infiltration anesthesia. Exploration ruled out the possibility of the huge mass being a cyst. The patient was then anesthetized with cyclopropane, and a blood transfusion was begun. The incision was extended to the xiphoid process and the symphysis pubis. Every accessible blood vessel to and from the tumor was clamped, severed, and ligated with catgut. The greatly distorted bladder was retracted near the symphysis pubis. The right ureter measured about 2.5 cm. in diameter. Multiple adhesions were freed. The appendix appeared grossly normal. The left ureter was dilated less than the right. It was possible to clamp across the vaginal vault and remove the tumor in toto. The blood pressure fell to 60/40, and the pulse

increased to 135; however, the patient responded to ephedrine sulfate and increased rate of administration of blood.

The raw area exposed was tremendous. The kidneys, liver, spleen, stomach, and intestines had been markedly displaced upward, and showed the effects of pressure. Hot packs were used to control oozing from the areas which could not be sutured or ligated. Fortunately, sufficient peritoneum had been removed from the tumor to permit very satisfactory covering of denuded areas. The peritoneum and fascia were closed with four sutures of chromic catgut. Six tension sutures of silkworm gut were employed. The skin was sutured interruptedly.



Fig. 3.—Six months postoperatively. Patient weighed 124 pounds.

Following a pressure dressing, two sand bags were applied. The operating time was sixty-five minutes. The blood pressure was 100/65 at the end of the procedure.

The pathologist, Dr. Emma Moss, reported as follows: The specimen consisted of a huge mass, weighing 55 pounds and being 17 inches in its greatest diameter. It had been bisected, and was solid except for a few very small cystic areas filled with a light yellow to reddish fluid. In many areas it showed evidences of degeneration. It presented a general appearance of having been encapsulated. A tube and somewhat cystic ovary could be identified. The opposite ovary was thinned out by the mass to such an extent that only a prolonged remnant remained. One surface of the uterus could be identified, and it evidently was the site of origin of the tumor. The outer surface was smooth and red. Final corrected microscopic diagnosis: "Leiomyoma with degeneration. Acute and chronic inflammation. No evidence of malignancy."

After the first four uneventful postoperative hours, the blood pressure suddenly dropped to 90/60, and 500 c.c. of citrated blood were administered to supplement the 1,000 c.c. received on the operating table. After two hours the blood pressure returned to a satisfactory level. Intravenous fluids were administered. Wangensteen suction was employed for the first two days. After twenty-four hours the sand bags were removed from the abdomen. On the third postoperative day the patient was afebrile, with a soft abdomen, and appeared clinically much improved.

On the fifth postoperative day the patient received 500 c.c. of plasma during the morning, after her serum protein was found to be 4.4. That night, after having received 250 c.c. of plasma, she experienced a chill with temperature going to 105° F., the pulse rate to 140 per minute, and the blood pressure dropped to 50/30. Adrenalin, morphine, and oxygen were administered. She was dyspneic, cyanotic, and unconscious, with râles in her lungs. Digalen was begun. Roentgenography revealed cardiac enlargement and passive congestion of both lungs. Electrocardiography revealed low amplitude of complexes compatible with congestive failure.

The following day the patient developed diarrhea. No evidence of cul-de-sac infection was found. Studies of the stool revealed atypical Shiga paratyphoid and atypical Salmonella paratyphi. The urine contained numerous blood cells. The patient's condition gradually improved. On the eleventh postoperative day, after all sutures had been removed and an abdominal binder had been applied, the patient was allowed up in a wheel chair.

On the twenty-fifth postoperative day the patient weighed 70 pounds, and she was able to walk with assistance. One week later she was discharged, free of edema, and weighing 75½ pounds. Six months later she weighed 124 pounds. The circumference of the abdomen was 34 inches.

When last seen (Jan. 23, 1947) she was in excellent physical condition for the age of 63 years.

Summary and Conclusions

1. The history of uterine myomas constitutes one of the most fascinating chapters in the story of gynecology.

2. Successful removal of uterine myomas weighing more than 25 pounds has been authentically reported by Hill,¹ Webster,² Cullen,³ Farmer,⁵ Marshall,⁶ and Stevens.⁷ The tumors in the cases of Webster² and Cullen³ weighed 87 and 89 pounds, respectively, and were cystic.

3. The solid myoma in the case herewith reported weighed 55 pounds and measured 17 inches in diameter. The patient is enjoying excellent health four years after operation.

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LEIOMYOFIBROMA OF THE UTERUS AND ENDOMETRIAL CARCINOMA*

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A NUMBER of statements in the literature refer to the frequent occurrence of leiomyofibroma of the uterus with endometrial carcinoma of the uterine body. Considerable importance has been ascribed to this association, not only in regard to certain clinical considerations in affected patients, but also as indicating a possible etiologic relationship between the conditions. On the other hand, a few authors have expressed skepticism regarding any real significance to be found in the coexistence of the tumors. Several have even doubted any connection whatsoever between the two, and, among other points, have made mention of the clinical impression that fibroids of the uterus are frequently present without, as well as with, endometrial carcinoma. However, actual statistical facts regarding this controversial matter seem to be largely lacking.

Forty-five years ago Cullen¹ noted that a large percentage of his cases with carcinoma of the uterine body also had fibromyomas. However, he stated that myomas were so common that the high incidence here was not surprising. Meigs,² in addition to citing statistics from the literature, gave the occurrence of uterine fibroids with endometrial carcinoma at the Massachusetts General Hospital as 20.8 per cent. Other reports on the coexistence of fibroids with carcinoma give such high percentages as 34.9 by Norris and Dunn;³ 38, Healy and Brown;⁴ 36.4, Masson and Gregg;⁵ and 37.8 by Scheffey, Thudium, and Farrell.⁶ From the other point of view, that is, regarding the incidence of carcinoma among fibroid uteri, the statistics, though considered significant, are not so striking. For example, in 1909 Kelly and Cullen,⁷ among 1,400 myomatous uteri, found 25 or 1.7 per cent to have corpus carcinoma also. Figures given by other authors all remained within the vicinity of 1 or 2 per cent, except for the surprisingly high percentage of 9.9 in a small series reported by Falls.⁸

An important clinical feature of the frequent coexistence of fibroids and endometrial carcinoma was indicated by Scheffey, Thudium, and Farrell⁶ when they stated that too often menorrhagia and metrorrhagia were ascribed to the presence of the fibroids with consequent disregard of the malignancy possibility. Also, the frequent coexistence of fibroids would seem greatly to affect the accuracy of attempts at estimating the extent of the malignant growth on the basis of the size of the uterus, as suggested by Healy and Brown.⁴ Of interest in another direction is the fact that the frequent finding of uterine myomas with endometrial carcinoma has led to considerable speculation regarding some etiologic connection between the two. Meigs,² granting the possibility that the presence of fibromyomas might lead to carcinoma, believed, however, that the association was more likely due to the ability of some uteri to develop malignant as well as benign tumors. To Novak,⁹ although agreeing in general with Meigs,

*Presented before the Central Association of Obstetricians and Gynecologists, Fourteenth Annual Meeting, Chicago, Ill., Sept. 19 to 21, 1946.

it also seemed logical to suppose that an irritative effect of fibroids, especially the submucous variety, might produce some predisposition to endometrial malignancy.

Recently, with the great interest in endocrinology, there has been considerable conjecture regarding an explanation of the frequent association of the growths on the basis of a common etiologic factor in the nature of internal glandular dysfunction. Particularly mentioned as a possibility has been excessive estrogen effect. In support of the fibromyoma side of the picture, much has been said regarding the work of Nelson¹⁰ and others in the experimental production of fibroid uterine nodules in animals by abnormally high or unopposed estrogenic effect. Interesting as may be the possibilities of these experiments, it should be remembered that the artificially produced nodules have only some resemblances to fibromyomas and are not complete duplicates.¹¹ Moreover, there appears as yet to be no unequivocal or clear-cut experimental, clinical, or statistical evidence favoring a speculative connection between estrogenic action and uterine fibroids as found in women. Consequently, the frequent finding of fibromyomas with endometrial carcinoma cannot as yet be considered reliable support for the rather commonly believed in, but still largely hypothetical, estrogenic etiology of the latter condition.

The foregoing is far from a complete survey of the literature on the subject of uterine fibromyomas and endometrial carcinoma, but it does give some illustrative examples of the extensive speculation and investigation which have been devoted to the connection between the two growths. After critically reviewing this material, interesting and thought provoking as it may be, it appears that one might well inquire as to why all this theoretical work has been undertaken when one fundamentally basic fact seems as yet not to have been established. I refer to the lack of good and substantial evidence that carcinoma of the uterine body has a disproportionately higher incidence among fibromatous than among the nonfibroid uteri of a series of cases. Or, looked at from the other direction, one searches in vain for satisfactory proof that fibromyomas, though admittedly frequently associated with endometrial carcinoma, are in fact more often found with that growth than in instances, comparable as to age and other factors, where it is not present. Actually, there is a remarkable dearth of studies regarding the point. Having some bearing on the matter were certain data which we obtained incidentally in the investigation¹² of another subject, and which failed to suggest any increased incidence of leiomyofibroma with endometrial carcinoma. Because of small numbers, however, as well as other reasons, definite conclusions could not be drawn, and a more extensive examination seemed indicated. Consequently, a study was made of a substantial series of cases with hysterectomy from Harper Hospital.

At this hospital during the five years from 1939 through 1943 there were 2,246 abdominal hysterectomies which were done on various indications. Of this number, there were 1,389 with fibromyoma as a primary diagnosis, either alone or in combination with other conditions. Presumably in these cases the tumors were of definite clinical significance because of size, abnormal bleeding, pressure symptoms, or for other reasons. There were an additional 283 in which fibroids were mentioned in the secondary diagnosis. Together, then, there were 1,672 myomatous uteri, or 74.5 per cent of the entire series of 2,246. This

leaves 574, or 25.5 per cent, entirely free of fibroids, or at least without tumors of sufficient clinical importance or size to justify mention.

Included in the 2,246 hysterectomy cases were 44 in which carcinoma of the uterine body was present. (It should be noted that during the same five years at Harper Hospital there were 74 other cases of endometrial carcinoma, in which, however, hysterectomy was not done; but for various reasons [chiefly for hopelessly advanced disease] treatment was confined to irradiation therapy, or in a few instances to diagnosis only. These cases were not included in the studied series since knowledge of the presence or not of fibroids was dependent on ordinary pelvic examination, and was therefore far too subject to error for accurate statistical study.) These 44 cases treated by hysterectomy had for the most part also received preliminary irradiation, but, as this had been done within two months of operation in the vast majority, it could have had insufficient time for much effect on the size of fibroids where these were present. Finally, it is pointed out that the figures given here are very questionable as an indication of the actual incidence of endometrial carcinoma, but they are presented only as probably of considerable value in suggesting the relative occurrences with and without fibroids.

TABLE I. A FIVE-YEAR SERIES OF ABDOMINAL HYSTERECTOMIES SHOWING THE INCIDENCE OF ENDOMETRIAL CARCINOMA AMONG UTERI WITH FIBROMAS AND IN THOSE WITHOUT THESE TUMORS

	ALL CASES	WITH FIBROMAS	WITHOUT FIBROMAS
Hysterectomies	2,246	1,672	574
With endometrial carcinoma	44	15	29
Percentages	2.0	0.9	5.1

In Table I it is seen that the 44 instances of corpus carcinoma among 2,246 hysterectomies give an incidence of 2 per cent. For the 1,672 uteri with the diagnosis of fibromyoma, the occurrence of carcinoma was 15, or 0.9 per cent. This latter figure agrees fairly well (except for Falls's small series) with previous reports as given above in the discussion of the literature. However, among the 574 uteri of the series without leiomyofibromata, there were 29, or 5.1 per cent, with carcinoma of the endometrium. It is such comparisons which strangely seem to be lacking.

Since the foregoing findings were so contrary to what was to be expected from statements in the literature, a comparison in another direction seemed indicated as a check. For this purpose a group of uteri from patients with endometrial carcinoma was contrasted with another series of the same size which was comparable as to age and other factors, except that uterine malignancy was absent. Having some resemblance to this was a comparison by Meigs² of cases with uterine cervix carcinoma and others with carcinoma of the corpus. His study apparently showed a greater affinity of the latter for myomatous uteri since the ratio of carcinoma of the body to that of the cervix was increased from 1 to 3.7 in general occurrence to 1 to 2 in cases with fibroid uterus. However, such an important factor in the incidence of fibroids as the ages of the members of the groups was apparently not considered. Moreover, it is not clear

whether or not the groups were compared on the basis of data obtained from ordinary pelvic palpation or by accurate examination of excised organs. In the present study the previously used 44 instances of endometrial carcinoma treated by hysterectomy were increased to 50 by the addition of 6 similar cases from the complete year 1938 and the first 2 months of 1944. According to age the 50 women fell into ten-year groups as follows: 30 to 39 years, 2; 40 to 49 years, 13; 50 to 59 years, 23; and 60 years and over, 12.

The 50 cases for contrast with the endometrial carcinoma series were found after a search through the abdominal hysterectomy records for the five-year period 1939 through 1943, plus approximately the first half of 1944. In order that there could be no question of padding, so to speak, of this group with a disproportionate number of fibromyomatous cases, only those instances were included in which the uteri were removed for reasons *other* than fibroids. Actually, the indications were as follows: pelvic relaxation, malposition, etc., 16; ovarian tumors—malignant, 9, and benign, 3; pelvic inflammatory disease, 9; functional bleeding, 6; unexplained postmenopausal bleeding, 3; endometrial polyp, 3; and adenomatous polyp of the cervix, 1. In addition to comparable ages for the two groups, there was also a rather close correspondence in other respects. For example, in the carcinoma group 47 were married and 36 of these gave a history of one or more pregnancies; whereas, in the other series the figures were 48 and 39 respectively. Again, of the 50 women with carcinoma, there were 16 who were, or at least considered themselves to be, still menstruating; while in the other group there were 19. It is perhaps worthy of mention that there was no necessity to take into consideration the influence of race, since all but 3 of the 100 women in the two groups were Caucasians.

TABLE II. OCCURRENCE OF FIBROIDS IN 50 UTERI WITH ENDOMETRIAL CARCINOMA AND A SIMILAR GROUP OF CASES AS TO AGE, ETC., WITHOUT CANCER OF THE UTERINE FUNDUS

	WITH FIBROIDS			
	SMALL	(SIZE OF 12 TO 16 WEEKS' PREGNANCY)	LARGE	TOTAL
50 with endometrial carcinoma	14	2	2	18 (36%)
50 without endometrial carcinoma	17	4	2	23 (46%)

In Table II is the comparison of the two groups showing the number of fibroid and nonfibroid uteri. The former are further analyzed roughly as to size of the tumors, the estimations being based on statements of the operators and measurements taken in the laboratory. In every instance there is a fairly close agreement between the two series, rather than an increased incidence of fibromyomas for the cancer group, as might be expected from certain statements in the literature. Indeed, it is slightly higher for the noncancer cases. This fact assumes greater significance when it is recalled that in the latter group the indications for hysterectomy were conditions *other* than fibromyomas in all instances. These data largely confirm the results of the first comparison, and cer-

tainly offer no evidence favoring the idea of a connection between fibromas and carcinoma of the uterine body, but rather just the opposite.

Summary

The frequent coexistence of fibromyomas of the uterus and endometrial carcinoma has been the subject of considerable conjecture and investigation regarding its significance from both clinical and etiologic standpoints. It has never been satisfactorily established, however, that the high incidence of fibroids can be considered as peculiar to or characteristic of corpus carcinoma, and not just simply a reflection of the frequent occurrence of fibromyomas. In order to remedy the surprising dearth of information on this essential and basic point, a study was made of hysterectomies at Harper Hospital. Among 2,246 consecutive abdominal hysterectomy cases there were 44 with endometrial carcinoma, an incidence of 2 per cent. In this series there were 1,672 with a diagnosis (1,389 primary and 283 secondary) of fibromyomas, of which only 15, or 0.9 per cent, showed carcinoma. In marked contrast, the group of 574 without fibroids had an incidence of 29, or 5.1 per cent, with uterine fundus cancer. As a check on this unexpected finding, a series of 50 endometrial carcinoma cases were compared with a like number of noncancerous instances, falling into the same age groups, and in whom the operations had been done for various reasons other than fibromyomas. Of the carcinomatous uteri there were 18 with fibroids, while in the other group the number was 23. There is no evidence in these data to indicate that fibromyomas of the uterus and endometrial carcinoma have an affinity for each other, but rather the reverse.

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A STUDY OF THE INTER-ACTION OF PREGNANCY AND HYPERTENSIVE DISEASE*

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WHILE there have been several studies of the effect of hypertensive disease upon pregnancy, there seems to be but little known of the effect of pregnancy upon the hypertensive disease. It is recognized that pregnancy is immediately hazardous to the hypertensive woman and to her fetus, and it has been surmized that once through the pregnancy, the mother has suffered irreparable damage which shortens her life expectancy. This supposition does not appear to be buttressed by solid evidence.

In the present paper, we shall report our findings in all patients aborting or delivering in this hospital, in whom the diagnosis of hypertensive disease could be established from blood pressures recorded before the twenty-fourth week of gestation. The fact that therapeutic abortion was done in only three of the 301 pregnancies gives us an almost unique opportunity for studying the interaction of pregnancy and hypertensive disease. In the follow-up of patients, we have traced every patient to 1946.

Stander and Peckham¹¹ followed up 57 per cent of their patients who were diagnosed as having "nephritis complicating pregnancy," and found a mortality of 40 per cent among those traced. While they felt that pregnancy had aggravated the disease and hastened the end, they were unable to prove this. Browne and Dodds^{1,2} followed 65 patients with hypertensive disease, and came to the conclusion that the large majority could pass through several pregnancies successfully and without any demonstrable deterioration in their condition. Reid and Teel¹⁰ in studying 122 patients with hypertensive disease, could not "find enough evidence to justify radical interference in patients already pregnant, with mild asymptomatic hypertension, normal hearts and kidneys." Wellen, Welsh, and Taylor¹³ followed six women with hypertensive disease through seven pregnancies, and for periods up to four years post partum. They found no evidence that pregnancy had any deleterious effect as judged from blood pressure, renal blood flow, or diodrast Tm (normal tubal excretory capacity).

Material and Methods

We have searched through all charts bearing the diagnosis of "toxemia of pregnancy," covering the period from the opening of the hospital in October, 1931, through 1944. There were 218 patients seen here in 301 pregnancies

*The Prize Award Thesis presented at the Fifty-Seventh Annual Meeting of the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons, Hot Springs, Va., Sept. 5 to 7, 1946.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

classifiable as hypertensive toxemia. While there must have been many more cases, we have taken only those in whom (a) hypertension was known to have existed before pregnancy, or (b) hypertension was found before the twenty-fourth week of gestation, no previous normal readings having been recorded during the pregnancy. Our standard for hypertension is 140/90 or greater. Patients showing hypertensive levels of blood pressure only at the initial clinic visit were excluded. Recognizable cases of glomerulonephritis and pyelonephritis were rejected; however, 15 patients (7 per cent of the series) were classifiable as renal disease. We believe that these are cases either of nephrosclerosis secondary to the hypertensive disease, or with superimposed pre-eclampsia.

Our postpartum toxemia clinic records have been of great value, in that they have given us repeated blood pressure readings while the patients were not pregnant. We recently have looked through the record room files of every hospital in Hudson County, and whenever we found an admission of one of our patients, before or after she came into our hands, we have studied her hospital chart.

At follow-up, we have determined the blood pressure, by mercury sphygmomanometer, with the patient sitting, and (usually) again, after examination and quiet reassurance, with the patient lying down. The lower reading is reported. The diastolic pressure was taken as the point at which the pulse sounds suddenly became dull and muffled. The eyegrounds were examined without mydriasis. A palpatory estimation was made of the state of the radial arteries, and the heart was auscultated. Cardiac size was determined by x-ray. The morning urine was examined for protein, sugar, specific gravity, and formed elements. Unless the specific gravity of protein and sugar-free urines exceeded 1.022, urea clearances were done. Blood chemical determinations included sugar, nonprotein nitrogen, and urea.

The Hazards of Pregnancy

Since a detailed analysis of the 301 pregnancies was published in the March issue of this JOURNAL, we shall merely summarize our findings, which are in general agreement with the reports of others.

Nearly 40 per cent of our patients showed significant drops in the mid-pregnancy blood pressure. Often the pressure fell into the normal range. About half of the patients went through the entire pregnancy with essentially constant blood pressures. Near delivery, the blood pressure was increased over the initial levels in 30 per cent of cases.

The outstanding hazard of pregnancy is the superimposition of toxemia, which occurred in about 30 per cent (by our criteria: increase in blood pressure and appearance of proteinuria, or marked proteinuria alone, or edema in combination with either of the above or toxemic symptoms). The incidence of eclampsia in these hypertensives was exactly 10 times that in all patients, while the incidence of pre-eclampsia was increased seven times. We could find no satisfactory criteria by which to judge the likelihood of toxemia occurring. It is somewhat more common in young primiparas, and has a recurrence rate of close to 70 per cent in later pregnancies. Its incidence bears no relation to the severity of the original hypertension.

There were six immediate maternal mortalities, four of which occurred in the first pregnancy definitely classifiable as hypertensive. In addition, seven women died within the first four months post partum. These 13 deaths give a maternal death rate of 4.3 per cent, or 20 times that for all patients in this clinic. Two of the deaths followed abortion—one therapeutic and one spon-

taneous. Of the 13 deaths, eight were attributable to hypertensive disease, and five were chargeable to intercurrent causes.

The gross fetal loss in the 301 pregnancies was 38.2 per cent. In the 840 pregnancies occurring before the establishment of the diagnosis of hypertensive disease, the fetal loss had been 34.7 per cent. In 127 later pregnancies, it was 40.2 per cent.

The fetal mortality increased with increasing severity of the hypertension, with the appearance of proteinuria, with renal impairment, and especially with the superimposition of pre-eclampsia or eclampsia.

These data certainly establish the dangers of pregnancy itself—one woman in 23 died, and two in five lost their babies. Yet the majority of hypertensive women apparently are not jeopardized by pregnancy. Two thirds of our patients escaped superimposed toxemia. In this group, there were no immediate maternal deaths, and one of the two late puerperal deaths was of intercurrent causation. The fetal loss was 18.5 per cent. Among the one-third of patients who had pregnancies complicated by pre-eclampsia or eclampsia, there were six immediate maternal deaths (6.67 per cent), and five late puerperal deaths, giving a total maternal mortality of 12.2 per cent—10 times that in the uncomplicated hypertensive group. The fetal loss was exactly 50 per cent—almost three times that in the women who escaped superimposed toxemia. The follow-up findings to be presented indicate that repeated pregnancies are not remotely harmful to hypertensive women unless pre-eclampsia or eclampsia supervene.

If only we could determine which patients would escape superimposed toxemia, a good prognosis for pregnancy could be offered to two out of three hypertensive women. It is possible that the prompt termination of a hypertensive pregnancy at the first sign of developing toxemia would protect the patient from the dire possibilities which such toxemia carries. If this were so, then perhaps any hypertensive woman could be given a chance at pregnancy, should she desire it. While her risks would be greater than those of a normal woman, there is a good chance that close supervision might give her the baby she wants.

Remote Mortality

Of the whole series of 218 cases, with *every patient* traced to late 1945 or 1946, 39, or 17.9 per cent, are dead. The length of follow-up varied from one to fourteen years, and averaged almost exactly seven years. Included in these 39 deaths are the six immediate and seven late puerperal deaths. Two of the immediate deaths will be considered as "remote" because they were associated with pregnancies subsequent to the one in which the diagnosis of hypertensive disease was established. All of the late puerperal deaths will be treated as remote, making 35 remote and 4 immediate fatalities.

The average age at death was 35.4 years; the ages ranged from 18 to 47 years. Of the 82 patients who had superimposed eclampsia or pre-eclampsia in 90 pregnancies, 26, or 31.7 per cent, are dead. In contrast, of the 136 patients who did not have superimposed toxemia, 13, or 9.6 per cent, are dead. The annual remote death rates were, respectively, 43.25 and 14.24 per thousand. For patients whose first observed blood pressure was 200 mm. Hg, or more, the annual death rate was 80.00 in contrast to 18.08 in patients whose initial pressures were less than 200. As for the 15 patients classified as having renal disease, 8, or 53 per cent, are dead (five of renal failure and three of cerebral hemorrhage). Urea clearances were done at follow-up in the seven survivors. Three clearances were less than 60 per cent, while four were 70 per cent or higher.

The causes of death, ascertained from hospital charts in 34 cases, and from death certificates in five, may be summarized as follows: Cerebral accident, 13; cardiac failure, 9; renal failure, 5; toxemia of pregnancy, 2; sudden death, 2 (ascribed to myocardial failure in the death certificates); and intercurrent, 8.

TABLE I. SUMMARY OF FOLLOW-UP FINDINGS IN 218 HYPERTENSIVE WOMEN

INITIAL SYSTOLIC BLOOD PRESSURE, MM. HG	140 TO 159	160 TO 179	180 TO 199	200 OR MORE	TOTALS
Cases	89	71	29	29	218
Dead, per cent	13.5	11.3	20.8	48.3	17.9
Annual death rate, per thousand	17.03		23.26	80.00	24.62
Percentage with aggravated hyper- tension at follow-up	46.4	30.3	28.6	26.1	36.3
Subsequent pregnancies, after orig- inal diagnosis of hypertensive disease (first year deaths ex- cluded)	42.5	38.8	46.4	29.2	40.3

Four of the intercurrent deaths were associated with pregnancy. One committed suicide four years after her second hypertensive pregnancy, one died of tuberculosis five and one-third years post partum, and two died of acute rheumatic endocarditis at three months and ten months after delivery, respectively. Thus 77 per cent of the deaths were associated with hypertensive disease (counting the sudden deaths as such).

The annual death rate, excluding the four immediate mortalities, was 24.62 per thousand, which is six times the expected rate for unselected urban women of the same age, color, and calendar year distribution.

Mortality tables were constructed exactly as outlined by Frost,⁸ with the exception that patients dying during a given year were recorded as having a full year's exposure. For comparison, we have used the Metropolitan Life Insurance Company's data on mortality among virtually unselected women insured on the weekly premium paying basis.

The death rates among our hypertensive women show no significant increase with age, in the age groups covered by this study. The ratio of actual to expected deaths, in fact, decreases with age—the older women seem to withstand the disease somewhat better than do the younger ones (Table III).

TABLE II. REMOTE MORTALITY IN HYPERTENSIVE WOMEN*

AGE AT DE- LIVERY	20 TO 24		24 TO 29		30 TO 34		35 TO 39		40 TO 44		TOTALS		
YEARS OF FOLLOW-UP FROM DE- LIVERY OF FIRST KNOWN HYPERTEN- SIVE PREGNANCY	PATIENT-YEARS EXPOSURE	DEATHS	PATIENT-YEARS EXPOSURE	DEATHS	PATIENT-YEARS EXPOSURE	DEATHS	PATIENT-YEARS EXPOSURE	DEATHS	PATIENT-YEARS EXPOSURE	DEATHS	PATIENT-YEARS EXPOSURE	DEATHS	ANNUAL DEATH RATE PER 1,000
1	20.0	0	60.0	1	46.0	4	57.0	1	30.0	1	213.0	7	32.86
2	19.5	0	57.5	2	41.5	1	53.5	1	29.0	0	201.0	4	19.90
3	19.0	1	53.5	2	38.5	0	47.5	0	26.5	0	185.0	3	16.22
4 to 6	41.0	1	120.0	1	94.0	1	119.0	2	52.0	3	426.0	8	18.77
7 to 9	21.0	2	79.5	1	66.5	2	76.5	3	27.5	0	271.0	8	29.52
10 to 12	7.0	0	25.0	0	30.5	3	26.0	1	20.0	0	108.5	4	36.36
13 to 14	1.0	0	5.0	0	2.0	0	3.0	0	3.5	0	14.5	0	0.0
Totals	128.5	4	400.5	7	319.0	11	382.5	8	188.5	4	1419.0	34	23.96

*Follow-up reckoned from time of delivery of first pregnancy in which diagnosis of hypertensive disease was established. Omitted: Four immediate maternal mortalities, and the case of a 16-year-old girl who died two and one-half years after delivery.

TABLE III. REMOTE MORTALITY IN HYPERTENSIVE WOMEN, IN RELATION TO PREGNANCIES SUBSEQUENT TO THE ONE IN WHICH THE DIAGNOSIS OF HYPERTENSIVE DISEASE WAS ESTABLISHED*

ATTAINED AGE	ALL PATIENTS							NO SUBSEQUENT PREGNANCY			ONE LATER PREGNANCY			TWO OR MORE LATER PREGNANCIES		
	EXPECTED ANNUAL DEATH RATE PER 1,000	PATIENT-YEARS EXPOSURE	ACTUAL DEATHS	EXPECTED DEATHS	RATIO OF ACTUAL TO EXPECTED DEATHS	ACTUAL ANNUAL DEATH RATE PER 1,000		PATIENT-YEARS EXPOSURE	DEATHS	ANNUAL DEATH RATE PER 1,000	PATIENT-YEARS EXPOSURE	DEATHS	ANNUAL DEATH RATE PER 1,000	PATIENT-YEARS EXPOSURE	DEATHS	ANNUAL DEATH RATE PER 1,000
20-29	2.460	276.5	0	0.68	8.8	21.70		116.0	4	34.48	115.0	3	26.08	76.0	1	13.16
30-39	3.283	602.5	14	2.17	6.5	21.13		370.5	9	24.28	365.5	4	10.94	158.0	3	18.98
40-49	5.384	453.0	14	2.42	5.8	30.90		309.5	10	32.29	308.5	9	29.18	101.0	3	29.70
50-59	9.412	27.0	0	0.24	1	0.0		25.0	0	0.0	25.0	0	0.0	2.0	0	0.0
Total	3.952	1419.0	34	5.6	6.1	23.96		821.0	23	28.02	814.0	16	19.66	337.0	7	20.78
Standardized death rates								28.36		19.49		20.90		261.0		15.32
																10.77

*Four immediate mortalities were omitted and the case of a 16-year-old girl who died two and one-half years after delivery.

The death rate is highest in the first year post partum, because of the late puerperal mortalities. After the sixth year of follow-up, the death rate again increases (Table II).

The Effect of Repeated Pregnancies.—The patients were divided into three groups:

A. Those who have had no pregnancy subsequent to the one in which the diagnosis of hypertensive disease was established.

B. Those who had one later pregnancy, and

C. Those who had two or more later pregnancies.

Table III shows that the annual death rate is not affected by repeated pregnancies, even with the risk of superimposed toxemia in the later pregnancies. Admittedly, the women having later pregnancies may be a select group. We have, therefore, sought in various ways to correct for this factor of selection.

As a first approach, we have excluded first year deaths in making a separate calculation of the death rates in women having no later pregnancy (Table III). Thus all the cases represented in this column of the table have survived for at least a full year after delivery.

A direct method of determining the effect of later pregnancy is to calculate the death rates based upon periods of follow-up from the second, third, and fourth pregnancies, rather than from the delivery of the first known hypertensive pregnancy (Table IV). Inherently, however, the effect of this method is to retain all of the deaths, while shortening considerably the follow-up periods. That is, the more pregnancies the patients have, the higher the calculated death rates will be. Also, such calculation deals with women who are getting older, and who have had their hypertensive disease longer. Despite this stacking of the cards against the apparent conclusion to be drawn from Table III, we again find that repeated pregnancies have not increased the annual death rates. The patients with three or more pregnancies are so few that the death rate shown in line 12 of Table IV cannot be considered reliable, especially since one of the deaths was intercurrent.

TABLE IV. REMOTE MORTALITY RATES IN HYPERTENSIVE WOMEN HAVING REPEATED PREGNANCIES*

	PATIENT-YEARS EXPOSURE	DEATHS	ANNUAL DEATH RATE PER 1,000
1. No later pregnancy	824.0	24	29.14
2. Later pregnancy (ies), interval from delivery to first later conception	163.0	0	0.0
3. 1 plus 2	987.0	24	24.33
4. One later pregnancy; conception to follow-up observation	214.5	7	37.29
5. Two or more later pregnancies; interval from first to second conceptions	70.5	0	0.0
6. 4 plus 5	285.0	7	24.56
7. Two later pregnancies; interval from second conception to follow-up observation	96.0	1	10.41
8. Three or more later pregnancies; interval from second to third conceptions	21.0	0	0.0
9. 7 plus 8	117.0	1	8.55
10. Three later pregnancies; interval from third conception to follow-up observation	27.5	3	
11. Four or more later pregnancies; interval from third to fourth conceptions	5.5	0	
12. 10 plus 11	33.0	3	90.91
13. All cases with later pregnancy; interval from first later conception to follow-up observation	435.0	11	25.28

*Mortalities reckoned from periods of follow-up after the later pregnancies, in an effort to determine the effect of the pregnancy.

Since the highest death rate was found in the women with initial blood pressures of 200 mm. Hg or more, the question rises as to whether these patients escape later pregnancies, and contribute unduly to the mortality in our Group A (no subsequent pregnancy). Table V shows separately the relation between subsequent pregnancies, and the annual death rates for patients with initial blood pressures of less than and more than 200 mm. Hg. In those women whose initial pressures were 200 or higher, repeated pregnancies are associated with a somewhat lower death rate than is found in patients having no later pregnancy. However, the cases are too few to permit any definite conclusion. In the milder hypertensives, repeated pregnancy is associated with a slightly increased death rate. Two of the remote deaths occurred in later pregnancies (one being a rupture of the uterus), and might be considered as coming under the hazards of pregnancy itself. Without these deaths, the annual death rates would be slightly lower for women with pregnancies subsequent to the one in which the diagnosis of hypertensive disease was made.

TABLE V. THE RELATION BETWEEN REPEATED PREGNANCIES AND THE ANNUAL DEATH RATE IN WOMEN WITH MILDER AND MORE SEVERE INITIAL HYPERTENSION, RESPECTIVELY*

INITIAL SYSTOLIC BLOOD PRESSURE, MM. HG	LESS THAN 200			MORE THAN 200		
	PATIENT- YEARS EXPOSURE	DEATHS	ANNUAL DEATH RATE PER 1,000	PATIENT- YEARS EXPOSURE	DEATHS	ANNUAL DEATH RATE PER 1,000
All cases	1272.0	23	18.08	150.0	12	80.00
No later pregnancy, all cases	717.5	14	19.52	106.5	10	93.90
No later pregnancy, excluding first year deaths	713.5	10	14.02	103.5	7	67.62
Later pregnancy, all patients	554.5	9	16.22	43.5	2	45.97
Later pregnancy, ex- cluding two deaths in pregnancy	552.5	7	12.66	43.5	2	45.97

*Four immediate maternal mortalities were omitted.

Another factor of selection lies in the relative numbers of patients who have pregnancies following hypertensive pregnancies with and without superimposed toxemia, since posttoxemic women fare much worse than those who escape toxemia. Of the 82 women who had superimposed toxemia, 23, or 28.1 per cent, had later pregnancies. Of the 136 patients who escaped toxemia, 59 or 43 per cent, had later pregnancies. Thus our Group A (no subsequent pregnancy) is slightly weighted with posttoxemic patients who do poorly, and Groups B and C contain a selection of favorable cases. However, a separate analysis of patients with and without superimposed toxemia shows no significant differences in annual death rates for those who did and those who did not have pregnancies after the one in which the hypertensive disease was diagnosed.

In summary, during the period of follow-up (average seven years), repeated pregnancies in these hypertensive women have not significantly increased the annual death rate.

Severity of Hypertension at Follow-Up

Not all patients had hypertensive levels of blood pressure when re-examined. Twenty-six, or 11.9 per cent, had either a systolic pressure of less than 140 mm. Hg, or a diastolic pressure of less than 90 mm. Hg, or both. Of the 23 diastolic pressures below 90, 18 were in the 80's, and of the 17 systolic pressures below 140, 11 were in the 130's. Only two patients had pressures of less than 130/80 in both systolic and diastolic readings.

The follow-up findings will be presented in relation to superimposed toxemia, and to subsequent pregnancies. There are 199 cases, since we have eliminated the 11 immediate and late puerperal deaths from this analysis; five patients refused examination, and three died without follow-up blood pressure recordings.

Table VI shows the distribution of blood pressures at follow-up. Of 125 patients who did not have superimposed toxemia, only 8.0 per cent had systolic pressures of 220 mm. Hg or higher. Of the 74 patients who did have superimposed toxemia, 24.3 per cent had systolic pressures of 220 or greater. Analysis by the Chi square method shows that the difference is significant—there are only two chances in 1,000 that the disparity is not real. This finding is to be considered in the light of the fact that the superimposition of pre-eclampsia or eclampsia is not related to the initial level of blood pressure as found before pregnancy or in the first trimester. In other words, the hypertension seems to be worse after toxemia.

TABLE VI. THE DISTRIBUTION OF BLOOD PRESSURES AT FOLLOW-UP, CORRELATED WITH PRESENCE OR ABSENCE OF SUPERIMPOSED TOXEMIA, AND WITH SUBSEQUENT PREGNANCIES

SYSTOLIC BLOOD PRESSURE AT FOLLOW-UP, MM. HG	LESS THAN 179		180 TO 219		MORE THAN 220		TOTAL CASES
	CASES	PER CENT	CASES	PER CENT	CASES	PER CENT	
No superimposed toxemia, total cases	79	63.2	36	28.8	10	8.0	125
No subsequent pregnancy	53	64.7	20	24.4	9	11.0	82
One subsequent pregnancy	11	52.4	9	42.8	1	4.8	21
Two or more subsequent pregnancies	15	68.2	7	31.8	0	0.0	22
Superimposed toxemia, total cases	31	41.8	26	35.2	17	23.0	74
No subsequent pregnancy	14	37.8	14	37.8	9	24.4	37
One subsequent pregnancy	11	42.3	9	34.6	6	23.1	26
Two or more subsequent pregnancies	6	54.5	3	27.3	2	18.2	11
Totals	110	55.3	62	31.2	27	13.5	199
No subsequent pregnancy	67	56.3	34	28.6	18	15.1	119
One subsequent pregnancy	22	46.8	18	38.3	7	14.9	47
Two or more subsequent pregnancies	21	63.6	10	30.3	2	6.1	33

This is more clearly shown by a comparison of the follow-up blood pressures with the levels initially observed. A follow-up blood pressure was not considered as higher than the original one unless the difference was more than 20 mm. Hg. In patients who did not have toxemia, 30.6 per cent had greater hypertension at follow-up, while in those who did have superimposed toxemia, 46.1 per cent had increased hypertension. There are only 3 chances in 100 that this is not a real difference.

The relation between toxemia and the incidence of increased hypertension at follow-up is more evident in the patients followed for shorter periods of time. In order to have enough patients in each category, we have divided them into two groups: those followed less than six years, and those followed more than six years. It will be seen from Table VII that in the group followed more than six years there is not a significant difference in the incidences of increased hypertension as between patients with and without superimposed toxemia. For the shorter periods of follow-up, the posttoxemic patients do have a significantly higher incidence of aggravated hypertension. This is what might be expected if the toxemia contributes to the aggravation of the hypertension.

In our follow-up study of eclamptic and pre-eclamptic women we found,⁴ as had others, that the duration of the acute toxemia was very definitely correlated with the incidence of hypertension at follow-up. We have, therefore, sought for a relation between the duration of the superimposed toxemia and aggravation of the pre-existing hypertension. Our data are not ideal for this, because of the varying lengths of follow-up (many hypertensions become more severe with time). There were 55 cases for whom the duration of proteinuria

is known. Twenty-seven were carried for less than three weeks with proteinuria; 11, or 40.8 per cent, now have a greater hypertension than they had initially. In 28 cases, the proteinuria existed for more than three weeks; 17, or 60.7 per cent, now have an aggravated hypertension. The difference is not striking, since there are 13.5 chances in 100 that it may not be significant. The total maternal mortalities in the two groups are 18.5 and 25 per cent, respectively.

The initial level of blood pressure seems to have some bearing upon the incidence of increased hypertension following superimposed toxemia. As perhaps might be expected, a larger proportion (68 per cent) of mild hypertensives become worse (as judged by the blood pressure level). When the patients began with a severe hypertension, only 31 per cent became worse. This is shown in Fig. 1, which depicts the proportions of patients with aggravated diastolic hypertension. In those patients who escaped superimposed toxemia, the initial level of the diastolic pressure does not bear a significant relation to the incidence of increased hypertension as found at follow-up.

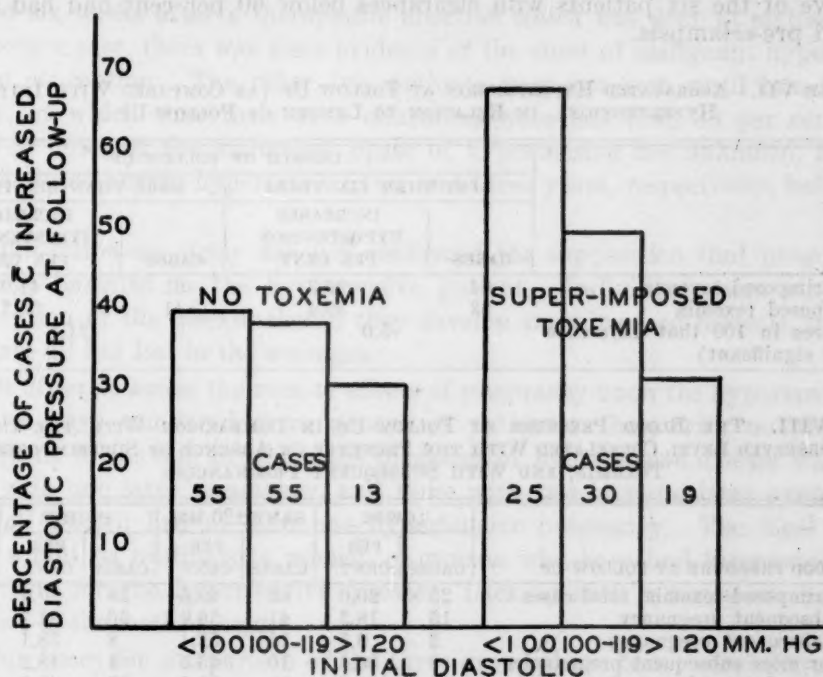


Fig. 1.

There was no relation between the patients' ages and the severity of hypertension at the time of re-examination.

It appears that repeated pregnancies do not result in an increased incidence of either severe hypertension or in aggravation of the hypertensions, even with the risk of superimposed toxemia (Tables VI and VIII). In fact, just as in the death rates, the patients having two or more subsequent pregnancies are, on the average, somewhat better off than those having one or no later pregnancy.

Proteinuria at Follow-Up

The voided urines of 194 patients were examined at follow-up. In 83.6 per cent, protein was either negative or present in only a "very faint trace," which is a normal finding by the sulfosalicylic acid method. Sixteen urines showed a

"trace" of protein (possibly significant), and 16 had 1 Gm. or more per liter. Of the 16 urines with significant degrees of proteinuria, 10 were terminal findings, and four others were those of patients in some degree of cardiac decompensation.

Renal Function at Follow-Up

In 72, or 37.1 per cent, the urinary specific gravity was 1.022 or higher in casual urines. This we take to mean normal renal function³; the urea clearances done in 45 of these cases were all in the normal range. Urea clearances were done in 81 of the 122 patients whose urinary specific gravity readings were less than 1.022. There were only 14 clearances below 70 per cent, and eight of these were between 60 and 69 per cent.

Of the patients whose renal function was estimated, 96 per cent were normal. Four additional patients died of renal failure, and 21 others died without renal functional evaluation.

Five of the six patients with clearances below 60 per cent had had superimposed pre-eclampsia.

TABLE VII. AGGRAVATED HYPERTENSION AT FOLLOW-UP (AS COMPARED WITH INITIAL HYPERTENSION), IN RELATION TO LENGTH OF FOLLOW-UP

	LENGTH OF FOLLOW-UP			
	LESS THAN SIX YEARS		MORE THAN SIX YEARS	
	CASES	INCREASED HYPERTENSION PER CENT	CASES	INCREASED HYPERTENSION PER CENT
No superimposed toxemia	64	20.3	61	41.0
Superimposed toxemia	33	39.4	41	53.7
p (chances in 100 that difference is not significant)		5.0		21.1

TABLE VIII. THE BLOOD PRESSURE AT FOLLOW-UP IN COMPARISON WITH THE INITIALLY OBSERVED LEVEL CORRELATED WITH THE PRESENCE OR ABSENCE OF SUPERIMPOSED TOXEMIA, AND WITH SUBSEQUENT PREGNANCIES

BLOOD PRESSURE AT FOLLOW-UP	LOWER		SAME ± 20 MM.		HIGHER		TOTAL CASES
	CASES	PER CENT	CASES	PER CENT	CASES	PER CENT	
No superimposed toxemia, total cases	25	20.0	62	49.6	38	30.4	125
No subsequent pregnancy	15	18.3	41	50.0	26	31.7	82
One subsequent pregnancy	2	9.5	11	52.4	8	38.1	21
Two or more subsequent pregnancies	8	36.4	10	45.5	4	18.2	22
Superimposed toxemia, total cases	16	21.6	23	31.1	35	47.3	74
No subsequent pregnancy	9	24.3	11	29.7	17	46.0	37
One subsequent pregnancy	4	15.4	8	30.8	14	53.8	26
Two or more subsequent pregnancies	3	27.4	4	36.3	4	36.3	11
All patients	41	20.6	85	42.7	73	36.7	199
No subsequent pregnancy	24	20.2	52	43.7	43	36.1	119
One subsequent pregnancy	6	12.8	19	40.4	22	46.8	47
Two or more subsequent pregnancies	11	33.3	14	42.4	8	24.3	33

Subsequent Pregnancies

There were 127 pregnancies in 82 patients, subsequent to the one in which the diagnosis of hypertensive disease was made. The fetal loss in these later pregnancies was 51, or 40.2 per cent. Of these later pregnancies, 83 were delivered (or aborted) in this hospital, and are included in our analysis. The other 44 were either delivered or aborted at home or in other hospitals.

In the pregnancies which we saw, the recurrence rate of superimposed toxemia was 64 per cent. In pregnancies following nontoxic gestations, the incidence of superimposed toxemia was 25.4 per cent.

Discussion

Our analysis has confirmed what others have found about the immediate hazards of pregnancy, both to the hypertensive mother and to her fetus. The incidences of pre-eclampsia, eclampsia, maternal and fetal death are increased several fold. In our series, the maternal mortality in 301 hypertensive pregnancies was 4.3 per cent, including seven late puerperal deaths, some of which occurred elsewhere. This is 20 times the general rate in our clinic. Four of the late puerperal deaths were uremic, and it is quite possible that pregnancy may have accelerated the renal decompensation. However, one of these deaths occurred six weeks after a therapeutic abortion which was done at sixteen weeks. In another case, there was some evidence of the onset of malignant hypertension before conception. The other two patients were not seen until late in pregnancy, at which time their urea clearances were less than 30 per cent. The times of onset of the malignant phase of hypertension are unknown, although both had had severe hypertension two and three years, respectively, before conception.

Our follow-up study has not confirmed the supposition that pregnancy is remotely harmful to the hypertensive patient. Individual cases may suffer acceleration of the disease should they develop superimposed toxemia, but these cases are all but lost in the averages.

In order to assess the remote effects of pregnancy upon the hypertensive disease, we have compared three groups of patients: those with no pregnancy subsequent to the one in which the diagnosis of hypertensive disease was made, those with one later pregnancy, and those with two or more later pregnancies. Thus all women had at least one hypertensive pregnancy. The ideal control series would be nulliparous women, or women who have had therapeutic abortions done for the hypertensive disease. Lacking such a series, we have had to resort to the method used.

Our bases for comparison of the three groups have been: mortality, annual death rates, severity of hypertension at follow-up, proportions with follow-up blood pressures higher than the initially observed levels, and the renal, cardiac, and eyeground status. In the averages, repeated pregnancies are without demonstrable effect by any of these criteria.

As has already been pointed out, the major hazard of pregnancy in the hypertensive woman is the superimposition of toxemia. In addition to the increased maternal and fetal mortality which this complication carries, it also leaves some patients with severe and aggravated hypertension.

We cannot say that the pre-eclampsia caused the aggravation of the hypertension, for it is possible that the vascular system susceptible to toxemia is also more susceptible to the ravages of the hypertensive disease itself. Perhaps it is significant in this connection, that superimposed toxemia is more common in the younger hypertensives; it is well known that hypertension follows a more

serious course in the younger patients. If the toxemia *causes* the damage, then the prompt interruption of a hypertensive pregnancy at the first sign of developing toxemia should benefit the patient. Moreover, the courageous adherence to this policy would allow us to give any hypertensive a "trial of pregnancy." On the other hand, if the appearance of toxemia points to a vascular system which cannot withstand the hypertensive disease, then the prognosis is bad, regardless of pregnancy.

The midpregnancy drop in blood pressure has a very practical importance for diagnosis. An appreciable number of our hypertensives had perfectly normal blood pressures over several weeks of the second and third trimesters. Had their earlier hypertensive pressures been unknown, and had they first been seen in midpregnancy—as so many patients are—they would have been classified as pre-eclampsia. This factor also confuses the interpretation of permanent hypertension apparently left as a sequel of "pre-eclampsia."

Summary and Conclusions

From the opening of the hospital in October, 1931, through 1944, we have seen 218 patients in 301 pregnancies classifiable (from recorded blood pressures) as hypertensive toxemia.

Every patient was traced to late 1945 or early 1946. Of the 218, 39 are dead, 5 refused examination, and 178 were re-examined (four have died since re-examination).

The gross fetal loss:

In earlier pregnancies, 35 per cent

In the first hypertensive pregnancy, 38 per cent

In subsequent pregnancies, 40 per cent

Nearly 40 per cent of the hypertensive patients showed drops in blood pressure in midpregnancy.

Proteinuria occurred in half of the pregnancies.

Renal function tests were normal:

During pregnancy in 93 per cent

At follow-up in 96 per cent

The fetal mortality is increased by:

Higher initial blood pressures

Blood pressure rises in the second trimester

Higher pressures near delivery

Decreased renal function

Proteinuria

Superimposed toxemia

There were six immediate maternal deaths:

Four in first hypertensive pregnancy

Two in subsequent pregnancies

There were seven late puerperal deaths, making a total maternal mortality of 4.3 per cent, or 20 times the general rate for the same period.

The annual death rate of the 214 survivors was 24.62 per thousand, which is six times the expected rate for unselected women of the same age, color, and calendar year distribution.

In the 82 patients who had superimposed toxemia, the annual death rate was 43.25 per thousand, in contrast to 14.24 in patients who escaped toxemia.

Repeated pregnancies, even with the risk of toxemia, did not increase the death rate.

The superimposition of toxemia is followed by an increased incidence of severe and of aggravated hypertension.

Repeated pregnancies did not increase the incidence of severe, or of aggravated hypertension, despite the risk of toxemia.

The outstanding conclusion is that repeated pregnancies are not demonstrably harmful to the hypertensive woman. The pregnancy itself is hazardous should toxemia occur. Such superimposition of toxemia also does harm some individual patients.

We wish to express our gratitude to Dr. S. A. Cosgrove, Dr. J. F. Norton, and Dr. E. G. Waters for reading the typescript. Dr. Harry Perlberg read the chest plates, for which we are indebted to the x-ray department. Many physicians have given us permission to re-examine their private patients, and several doctors—as far afield as South Carolina—have examined patients for us. Mrs. E. H. Rafton, and especially Mr. M. Spiegelman of the Metropolitan Life Insurance Company have given us valuable help with the mortality tables. The superintendents and Record Room personnel of every hospital in Hudson County have cooperated in helping us to trace patients. Most of the urea clearances and blood chemistries were done by Misses Doris Furze and Eleanor Brudnicki, who also helped in checking hospital records.

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PLACENTAL METABOLISM OF VITAMIN C

II. Histochemical Analysis

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IN THE course of studying the placental metabolism of ascorbic acid, it becomes necessary to determine the localization of the vitamin within the tissues. The findings of Javert and Stander,¹ as well as of King,² imply an etiologic relationship between ascorbic acid levels and spontaneous abortion. Such a mechanism would presumably depend, however, more on the vitamin concentrations and (possibly) localization in the tissues involved, than simply on the levels discovered in the maternal plasma. Gross analyses have revealed no constant factor relating the maternal blood levels with placental concentrations of ascorbic acid³ and the present paper presents the corollary histochemical determinations.

Histochemical studies of the iron, glycogen, lipoids, phosphatase, and calcium content of the human placenta have been reported by Dempsey and Wislocki,^{4,5} and Gellhorn⁶ has recently demonstrated the cystologic aspects of sodium metabolism, using the radioactive ion. Ascorbic acid itself has been localized and studied in the adrenal, hypophysis, and ovary,⁷⁻⁹ Giroud and Leblond⁸ even demonstrating that the fixation of the vitamin in the corpus luteum undergoes a cyclic change as the lutein cells do. On approaching the problem in placental tissue, however, it proved necessary not only to establish the normal in the term placenta, but also to review critically the techniques available for ascorbic acid localization.

The reducing action of ascorbic acid on silver nitrate has provided the basis for most of the methods advanced for staining the vitamin. The difficulties attendant upon applying such a procedure to placental tissue fell into three groups: (a) the solubility of vitamin C in the various reagents used, (b) the degree of tissue penetration attained by the silver nitrate solution, and (c) the presence of other reducing substances in the placenta which might give false reactions. In the course of evaluating these difficulties and establishing a stain technique, over 500 placentas have been examined by one of us (J. H. H.).

Technique

1. A 2 to 3 millimeter slice of fresh placental tissue is cut by frozen section.
2. The tissue is floated onto 5.4 per cent levulose for ten minutes.
3. The tissue is placed in acidified silver nitrate solution and kept in the dark in an incubator at 56° C. for twenty minutes.
4. The impregnated tissue is washed in distilled water for fifteen to twenty minutes to remove the excess silver salts.
5. The silver stain is fixed in 5 per cent sodium thiosulfate for thirty minutes.

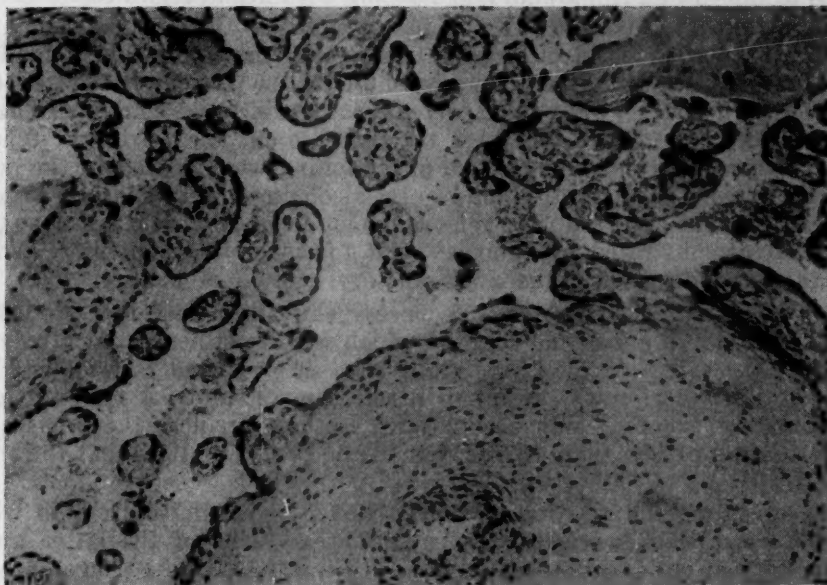


Fig. 1.—Section of placenta stained with hematoxylin-eosin without treatment with silver nitrate.

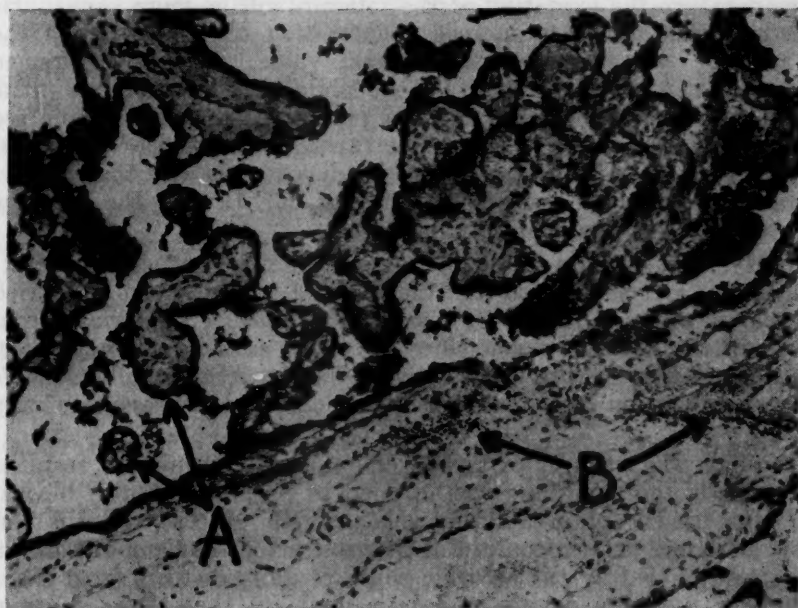


Fig. 2.—Silver nitrate stain, adjacent section of placenta. (A), Heavy deposition of ascorbic acid in syncytial layers. (B), Fine granules of stained ascorbic acid in stroma.

6. The tissue then is placed in absolute alcohol for twenty-four hours previous to embedding in paraffin and staining with hematoxylin-eosin.

Discussion of Technique.—Prior to establishing the above routine, every reagent or procedure used or feasible was tested for its tendency to dissolve vitamin C out of the tissues. One gram pieces of tissue were frozen on the frozen-section block, thawed, and assayed for ascorbic acid content. The mean loss was 6 per cent ± 2 , and, although the tissue so cut is exceedingly difficult to handle, this provided our best method of sectioning which assists in the penetration of the stain. Methyl, ethyl, and butyl alcohols were all checked as possible fixative agents, but were found to remove too much ascorbic acid from the tissues. It has been demonstrated by Bourne¹⁰ that formalin vapor interferes with the silver stain and does not make a satisfactory method of fixation.

Step 2 is necessary to remove excess chlorides, and the problem was presented of finding a washing solution which would neither remove the vitamin nor distort the cells. While 10 per cent levulose produced the smallest loss of vitamin C, its hypertonicity resulted in cell damage, and 5.4 per cent levulose (approximately isotonic) was used. With isotonic levulose there is loss of C from the tissues of less than 10 per cent in the period of time that the washing continues.

The silver nitrate solution of step 3 is a 5 per cent solution to which is added 0.5 c.c. glacial acetic per 100 c.c. The addition of the latter increases the specificity of the reaction, ascorbic acid being the principal substance which gives the argentaffin reaction in an acid medium. The 10 per cent silver nitrate recommended by Giroud and Leblond⁸ was found to give too much tissue distortion. A 5 per cent solution provides maximum impregnation with minimum cell distortion.

The incubation involved in the third step presented a problem. Admittedly at this temperature the oxidation of the vitamin will be more rapid. However, the procedure was found to increase penetration of the tissue by the silver nitrate, and for this purpose was of great value. It must be remembered, furthermore, that while the vitamin is heat labile, the vitamin-silver nitrate complex is not, so that as soon as the stain penetrates the microscopic section to reach the ascorbic acid, loss of the latter through elevation of the surrounding temperature ceases. After comparative studies it was felt that there was no appreciable loss from the twenty minutes of 56° C. and the penetration of AgNO₃ into the tissue was definitely increased.

Similarly, the vitamin-silver nitrate complex is not (in contrast to the vitamin itself) water soluble, so that the washing in step 4 can be carried out in distilled water without danger of loss of substance. Such washing must be carried out in the dark, however, since the silver salts have not yet been fixed. Absolute alcohol was selected as the tissue fixative (Step 6) because formalin causes the precipitation of a dense black artifact in the presence of any excess silver salt.

To evaluate the amount of reduction of the silver nitrate resulting from other substances, the technique was applied to prepared gelatin blocks. Four sections were used: plain gelatin, gelatin with glucose, gelatin containing glucuronic acid, and gelatin containing ascorbic acid. The amount and intensity of the color developed by the ascorbic acid are quite distinct from that formed by the weaker reducing agents, and it is doubtful that there is a significant amount of stain in the final sections which represents reduction of the silver salt by nonvitamin substances.

Results.—The photomicrographs in Figs. 1 and 2 indicate the typical distribution of the vitamin in placental tissue. From these it can be seen that the heaviest concentration of the ascorbic acid lies at the syncytial layer of the villi.

There is some C in the central core of the mesodermal connective tissue, as evidenced by an even distribution of granules. The granules in this area, however, are not as heavily deposited as at the syncytial layer. While the technique employed permits of quantitative conclusions only in the face of marked differences in staining, it was noted in all slides that the fetal portion of the placenta is richer in the vitamin than is the maternal portion.

Discussion

The distribution revealed in these studies is a reflection of the gradient of physiologic activity in the villus. Most of the metabolic function occurs at the syncytial layer, the area of maternal-fetal interchange, and in term placentas the principal evidences of degeneration and cytolysis lie in the center of the villi.

Bourne⁷ has stated that there is a perinuclear aggregation and an outlining of the Golgi apparatus and mitochondria by deposition of ascorbic acid granules. While this statement may or may not be true with respect to the adrenal, on the basis of the work here reported, it can be unequivocally denied with respect to the placenta. No perinuclear aggregation or definite intracellular localization is noted in any of the placental tissues examined, and it would seem remarkable if a substance as highly soluble as is ascorbic acid should follow a definite pattern of localization inside a cell. Furthermore, statements as to intracellular localization must be accepted with reservation until it can be demonstrated that the granules of silver nitrate do not migrate after precipitation. While such migration may occur intracellularly,¹¹ intercellular migration is doubtful, and the conclusions reached above as to the localization of the granules in various tissue areas undoubtedly represent the true distribution of the vitamin.

It is of interest to compare these findings with other reported localizations within placental tissue. Ribonucleoprotein and alkaline phosphatase are both also found predominantly in the syncytial layer. Their relationship is an inverse one, however, the ribonucleoprotein being high in early pregnancy and decreasing as the alkaline phosphatase rises.⁴ We have, in the course of this work, interrupted the pregnancies of rabbits at thirty and at sixty days for stains of the ascorbic acid in the placental tissue, and we can see no differences in concentration which can be related to the duration of the pregnancy.

Dempsey and Wislocki^{4, 5} have also postulated that the syncytium is the site of the production of placental steroids on the basis of histochemical evidence. They have observed in this layer a positive Schiff's reaction and a greenish fluorescence (both of which are abolished by preliminary treatment of the tissues with alcohol or acetone) as well as stainable fat droplets which are birefringent. Glycogen is not laid down primarily in the syncytial areas, being found principally where vascularization is poor and the oxygen tension low. Iron is distributed in both syncytium and stroma, not showing the sharp gradient which we have observed with ascorbic acid.

Summary and Conclusions

A modification of the silver nitrate method for the microscopic localization of vitamin C in tissues is presented. Application of this technique to the

human placenta reveals that the greatest concentration of ascorbic acid lies at the syncytial layer of the villus. A smaller portion was demonstrated within the stroma of the villus, but there is consistently more of the vitamin in the fetal than in the maternal portion of the placenta.

The histochemical studies here reported were carried out by Dr. Holzaeffel in partial fulfillment of the requirements for the degree of Master of Medical Science.

The authors wish to express their appreciation to Mrs. Rosalie York and Miss Eloise White for their technical assistance.

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PREGNANCY AND THE DOUBLE UTERUS

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ANOMALIES of the female reproductive system, manifested by various degrees of failure of fusion of the Müllerian ducts, are not uncommon, and many reports have been made in the recent literature. This paper is concerned only with the true double uterus with double cervix, an anomaly which is not seen frequently, and because the patient here reported has been observed during the courses of four pregnancies, it was thought worth while to report her case somewhat in detail. Of additional interest is the fact that she was seen during the course of a rather unusual illness prior to her first pregnancy.

It is important to have a clear understanding of what we mean by the term double uterus. Some writers include bicornate uterus and septate uterus in this general term. Taylor¹ makes a plea for a simple classification and suggests the following:

1. Uterus arcuatus
2. Double uterus with single cervix
3. Septate uterus with a single or a septate vagina
4. Double uterus with a double cervix
5. Uterus with a rudimentary horn or absence of one horn

This classification is far more simple than most offered, but still does not give as clear an anatomic picture as that of Way.² Way's classification is self-explanatory and obviates the possibility of any confusion.

1. Uterus arcuatus with a notch in the top of the fundus which does not extend through the entire thickness of the myometrium, and thus does not alter the conformity of the uterine cavity.
2. Uterus bicornis, unicorpus, unicollis, which as the name connotes means two cornua, one body, and one cervix.
3. Uterus bicorpus, unicollis. Two bodies and one cervix.
4. Uterus bicorpus, bicollis. Two bodies and two cervices.
5. Uterus sub-septus. One uterus which has an incomplete septum.
6. Uterus septus. One uterus with a complete septum which divides the uterine cavity and cervix in two halves.

Anomalies of the uterus may arise in one of three ways: (1) failure of fusion of the Müllerian ducts, (2) persistence of the median walls, and (3) through failure of development. Although the normal uterus is a midline organ, it is bilateral in origin and has a bilateral nerve and blood supply. Rudolph³ states that in the uterus simplex the fused medial walls of the Müllerian ducts are resorbed in a caudocranial direction. Arrest in the resorption of the fused medial walls at different levels gives rise to various types of anomalies. Failure of fusion of the Müllerian ducts is responsible for the true double uterus with double cervix. It is this particular type of deformity with which this paper is concerned.

Case Report

This patient was first seen Dec. 3, 1938. At that time she was 23 years old and had been married two months. She was admitted to the hospital because of severe lower abdominal pain, backache, nausea and vomiting, and diarrhea.

The onset of the illness was acute and was somewhat similar to food poisoning, and indeed this was the tentative diagnosis at the time of admission. She had begun menstruating at the age of 13 years, her periods were regular at intervals of twenty-eight days, the duration of flow was eight to ten days and the flow was rather profuse, requiring about 24 napkins during the entire period. There was only a moderate amount of cramplike pain during the first two days of the flow. Her last menstrual period had stopped about ten days before the onset of the present illness. General examination was negative, save for marked tenderness and some rigidity in both lower quadrants of the abdomen. Temperature on admission was normal, and the white blood cell count was 7,800 with a normal differential. The following day her temperature rose to 102° F., she continued to have vomiting and diarrhea, complained bitterly of cramplike pain in the lower abdomen and backache, and developed a rather profuse white vaginal discharge. The abdomen became rather markedly distended and tender, and it appeared as though there was a mass on either side of the midline just above the symphysis. Pelvic examination confirmed the presence of the masses, but there was such marked tenderness in the pelvis that a satisfactory examination could not be done. There was a rather abundant amount of white milky discharge exuding from the cervix. Repeated smears of this discharge showed only pus with very few organisms and no gram-negative diplococci.

The pain, backache, vomiting, and diarrhea persisted, and the abdominal distention became more marked. The stomach was kept emptied by means of continuous suction through a duodenal tube. It was obvious at this time that the patient had a pelvic peritonitis and there was a peculiar "doughy" sensation present upon palpating the abdomen. The possibility of a tuberculous peritonitis was considered, and during the fourth and fifth days of her illness this seemed the most likely diagnosis. She ran daily temperatures to 100° to 101° F., the white count remained within the normal range, the highest point reached was 9,200 on the seventh day of the illness, the pain and diarrhea persisted, and then on the eighth day of her illness she became suddenly better, her temperature gradually returned to normal and remained there. She was discharged from the hospital on the nineteenth day. She was afebrile during the last eleven days.

Following discharge from the hospital the patient returned rapidly to her normal health. The rapid recovery disproved our diagnosis of tuberculous peritonitis. It was doubtless that she had had a pelvic peritonitis, but the etiology was far from clear. It was not until about six weeks after her illness that a plausible cause was found. During the course of a pelvic examination, a small slitlike opening was seen on the left side of the vagina just inside the hymeneal ring. Exploration of this opening revealed another vagina, smaller than the one on the right, and further exploration revealed another cervix which was connected to the mass on the left side. Upon finding this anomaly in the pelvis, the theory was postulated that the patient had had a temporary blockage of the left side with retrograde menstruation into the peritoneal cavity. This opinion was substantiated to some degree at a later date when the patient had a cesarean section. The left tube was found to be patent with a delicate fimbriated end, but there were many weblike adhesions between the tube and broad ligament.

The patient was then seen in August, 1939, eight months after her illness, because of a period of amenorrhea of two months' duration. Her last menstrual period was June 7, 1939, and her expected date of confinement was March 14, 1940. On examination the right uterus was enlarged to about the size of an eight to ten weeks' pregnancy and was soft. The left uterus was slightly enlarged and was well out of the pelvis. Her antepartum course was not re-

markable, except for slight vaginal bleeding on one occasion at about ten weeks. On Dec. 30, 1939, when she was about twenty-six weeks pregnant, the left uterus was found to be partially in the true pelvis and exquisitely tender. On Feb. 27, 1940, two weeks before term, the head was dipping well into the pelvis, and the left uterus was entirely out of the pelvis. The patient went into labor spontaneously on March 11, 1940, and after an uneventful labor of eight hours delivered spontaneously a normal term female weighing 5 pounds, 14 ounces. There was no laceration of the perineum, but the septum was torn from its attachment to the anterior wall of the vagina. The placenta separated immediately and was expressed intact. There was no appreciable blood loss. The patient had an afebrile uncomplicated puerperium, and was discharged from the hospital on the fourteenth postpartum day.

Second Pregnancy.—On Dec. 9, 1940, nine months after her first delivery, the patient returned for care of her second pregnancy. Her last menstrual period was Sept. 7, 1940, and her expected date of confinement was June 14, 1941. On this examination the *left* uterus was found to be enlarged to about the size of a ten to twelve weeks' pregnancy. The right was also slightly enlarged but firm. Her antepartum course was normal and on April 26, 1941, approximately six weeks before term, the fetal head was well engaged in the pelvis and the right uterus was out of the pelvis. The patient then went into labor prematurely four weeks before term and, after an uneventful labor of six hours, delivered spontaneously a normal premature female weighing 4 pounds, 13 ounces. The placenta separated immediately and there was no appreciable bleeding during the third stage. Her puerperium was again afebrile.

Third Pregnancy.—The third pregnancy occurred while the author was in the service and no personal observation was made. In April, 1943, during her tenth week of pregnancy, the patient began to have vaginal bleeding which persisted for five days. On the fifth day she developed cramps on the right side and expelled a fetus with the placenta. Twenty-four hours later she developed cramps on the left side of her abdomen and expelled another fetus intact with the placenta. It was the impression of the physician who attended her that she was pregnant in both uteri.

Fourth Pregnancy.—The patient was first seen on Oct. 2, 1945, in the fourteenth week of her fourth pregnancy. The last period was on June 14, 1945, and the expected date of confinement was March 21, 1946. She gave a history of having passed about one-half cupful of clear fluid during the tenth week of her pregnancy, and had remained in bed for about a week because of lower abdominal cramps and the passage of fluid. On examination she was found to be pregnant in the left uterus, and the enlargement of the uterus corresponded with the period of amenorrhea. Her prenatal course was again essentially normal, with the exception of the fact that she had rather constant aching pains in the lower abdomen, particularly on the right.

At 4:30 A.M. on Jan. 25, 1946, in the thirty-second week of her pregnancy, she was suddenly awakened by a gush of blood estimated to be 50 to 60 cubic centimeters. A few minutes later she developed abdominal cramps and backache and passed what she thought was amniotic fluid. She was admitted to the hospital and given morphine in an attempt to prevent premature labor. A compatible donor was obtained and no rectal or vaginal examination was done. For the next ten days the patient continued to bleed moderately at intervals, particularly at night, and associated with the bleeding was regular and painful uterine contractions. She was given daily injections of estrogen and progesterone in an attempt to prevent premature labor, and on numerous occasions it was necessary to administer narcotics. The fetus was presenting by vertex and the head was floating above the pelvic brim. Finally, on the morning of February 3, approximately seven weeks from term, she developed hard labor pains

and began bleeding profusely. During the course of about an hour she passed approximately 600 c.c. of blood. Following the bleeding her membranes ruptured. The patient was given a transfusion of 500 c.c. of whole blood and, without anesthesia, a sterile vaginal examination was carried out. This examination revealed the fact that the right uterus was incarcerated in the hollow of the sacrum, down in front of the infant's head. The cervix of the pregnant uterus was long, dilated sufficiently to admit one finger, and placental tissue was felt over the internal os. In view of these findings, the decision was made to deliver the patient by section. Under local anesthesia, low-flap cesarean section was performed, and a normal premature male weighing 4 pounds, 6 ounces was delivered. The placenta was implanted on the lower uterine segment and partially covered the internal os. Inspection of the pelvis was interesting. There were two completely separate uteri with the pregnancy in the left uterus. The right uterus was slightly enlarged and was completely retroverted and lying in the hollow of the sacrum down in front of the presenting part of the infant. There was one normal tube and ovary on each uterus, on their lateral aspect. The left tube was adherent to the posterior leaf of the left broad ligament by several filmy weblike adhesions. The fimbriated end was delicate and patulous. There was a rudimentary round ligament on the medial aspect of the right uterus.

The patient had a very stormy convalescence complicated by atelectasis, bronchopneumonia, and a low grade peritonitis. The abdominal symptoms and findings were very similar to her first illness. She had severe abdominal cramps, diarrhea, vomiting, and the same "doughy" distention which characterized her first illness. Involution of both uteri was slow and there was never any evidence of passage of a decidual cast. She was finally discharged from the hospital on March 10, 1946. The baby did well, and upon discharge on April 12, 1946, weighed 9 pounds, 9 ounces.

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SPONTANEOUS ANNULAR DETACHMENT OF THE CERVIX DURING LABOR

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ANNULAR detachment of the uterine cervix occurring during labor is a rare complication. In 1933, DeCosta¹ collected reports of seventeen instances of this complication, including one of his own. In a thorough search of the literature, we have been able to find but fifty-four reported cases, and are reporting an additional instance which came under our observation.

The first recorded instance of this complication of labor was by Scott² in 1821. Including our own, there are but seven such cases occurring in the American literature, the first by Johnston³ in 1851.

We have omitted one case reported as occurring in a two months' abortion and one other complicated by carcinoma of the cervix occurring during labor which appears in Meigs⁴ textbook on obstetrics, published in 1856, as not being representative of spontaneous amputation occurring during labor.

Case Report

Mrs. H. J. S., aged 22 years, white, para i, gravida ii, was first seen prenatally on Sept. 11, 1944. At this time she was one month from term.

Her past obstetric history revealed that on Feb. 9, 1942, she had been delivered elsewhere by cesarean section. The indications given were "a difficult, prolonged labor, poor progress, a head in transverse arrest, and failure of the cervix to dilate satisfactorily after thirty-six hours of labor." The postoperative course was uneventful. The infant born in 1942 weighed 3825 grams.

The prenatal course of the pregnancy here reported was normal. The pelvic measurements were as follows:

I.S.—26 cm.

I.C.—29 cm.

I.T.—32.75 cm.

B.D.—21 cm.

D.C.—12.5 cm.

B.T.—10 cm.

Thom's x-ray pelvimetry was performed with the following results: anterior posterior diameter, 11 cm.; transverse diameter, 13 cm.

The fetus was in left occipitoanterior position, and was thought to be normal in size. Since there was no apparent cephalopelvic disproportion, a trial of labor was decided upon.

On Oct. 12, 1944, the patient entered the hospital in labor. The membranes were intact, the uterine contractions were occurring every four minutes, the cervix was undilated and uneffaced. The head was dipping into the pelvis but was unengaged.

After eight hours of labor, with strong uterine contractions every three minutes, the cervix was still undilated and was noted to be in the posterior part of the pelvis. After ten hours' labor, the head had descended somewhat into the pelvis but was above the spines. The cervix was effaced and 1 cm. dilated. After fourteen hours of labor, the membranes ruptured spontaneously. The uterine contractions were of good quality. The cervix was 3 cm. dilated. The head was at the spines. By this time it was decided that vaginal delivery could be anticipated. After fifteen hours of labor, the cervix was 3.5 cm.

dilated, and a small but continuous flow of blood appeared at the vulva. After twenty-two and one-half hours' labor, rectal examination revealed a fleshy mass in front of the head. The head had descended to well below the spines. At vaginal examination the mass was recognized as a detached annular portion of the cervix. The annular detachment was complete except for a 2.5 cm. tag of tissue at about 11 o'clock. After twenty-three hours of labor under ethylene anesthesia, the patient was delivered of a normal 3,300 Gm. female infant by low forceps in left occiput anterior position. The tag of cervix described above was clamped, cut, and tied.

There had been a moderate amount of vaginal bleeding during the last eight hours of the first stage. 750 c.c. of blood loss was collected in the delivery room. The estimate prior to delivery was 350 c.c., making a total of 1,100 c.c. blood loss during labor. The placenta separated spontaneously after 7 minutes of the third stage, and was expressed by modified Credè. The bleeding during the first stage probably came from the cervical lesion, with a small amount from the cervix during the second stage. The greater amount was from the uterus during the third stage.

Nineteen days post partum, a small rim of vaginal cervical tissue was present. On the patient's left, a tag remained about 4 millimeters in length. The artificial os admitted the tip of a finger.

Fourteen weeks post partum, the external os was rigid and very small. The patient had experienced three normal menstrual periods. She complained of an acquired dysmenorrhea that had increased since delivery.

Twenty months after delivery, the patient had avoided a repeat pregnancy. Her acquired dysmenorrhea was much less severe. The pelvic examination was essentially the same at this visit as when seen 14 weeks post partum.

Pathologist's Report.—The specimen consisted of a roughly hemispherical ring of dark bluish-red, rather friable tissue, measuring 5.5 cm. in diameter, with an opening 3 cm. wide. The tissue varied in thickness, with an average of 2 cm. Cut surfaces were solid, dark red, and friable after formalin fixation.

Sections cut parallel to the cervical canal showed a convex border covered by stratified squamous epithelium with transition to columnar cells and tubular glands at about the midpoint. The whole epithelial layer was stretched thin, and there was an infiltration of polymorphonuclear leucocytes and fibrin between the cells and on the surface. The lamina propria was fibrillary, markedly edematous, and sparsely infiltrated with leucocytes. The deeper structure was fibrous, with widely separated fibers with edema and extensive fresh hemorrhage between them. There were many distended, thin-walled blood vessels present, and the deep border of the tissue was made up of a fairly uniform layer of connective tissue strands and smooth muscle fibers, some lying parallel to the line of separation, while others appeared to have been disrupted tangentially or at right angles.

Pathologic Diagnosis.—Acute congestion, hemorrhage, and edema of cervix uteri, with spontaneous amputation of the pars vaginalis.

In this case, the cause given for cesarean section was "poor dilatation of the cervix." During the patient's second labor no apparent disproportion existed. The cervix was slow in dilating, and was definitely rigid. It tore away when the pains became hard following spontaneous rupture of the membranes.

One might believe that the starting point of separation would show an area where prolonged pinching had produced ischemia and necrosis. The detached specimen showed no area of necrosis along its peripheral edge, either grossly or histologically.

Analysis of Reported Cases

1. Seventy-five per cent of the cases occurred in primiparas.
2. The average age of the patients was 31 years.
3. The length of labor was given in forty-one instances. The average length of labor in these was fifty-eight hours. The longest labor was one hundred eight hours, and a total of nine labors were eighty hours or longer. There was one eleven-hour labor.
4. Twenty-eight case reports stated that the membranes ruptured prematurely or early. This means at least an instance of 48 per cent early rupture of the membranes. Some reports made no mention of the membranes. There were but six cases where the membranes ruptured late in labor.
5. In nine of the 55 cases, the authors stated that the pelves were contracted. In only six instances was "normal pelvis" definitely stated. This leaves forty cases where data upon the pelvis is not given. However, we note embryotomy listed under delivery in five cases where the size of the pelvis is not mentioned. This is suitable indirect evidence that contracted pelvis of some degree was present in another five cases, making a total of 14 cases, or over a 25 per cent instance of cephalopelvic disproportion.
6. The average weight of the babies, in 21 cases where those data were given, was 3,414 grams. Eight babies weighed 3,800 Gm. or more.
7. There were fifty-three vertex and two breech presentations, in both of which a rubber balloon was used.
8. Five cases of annular detachment of the cervix accompanied the use of an intrauterine hydrostatic bag. In the fifty remaining cases, spontaneous detachment occurred.
9. Seventeen authors made note of a "rigid cervix" to palpation, during the first stage of labor.
10. There were four maternal deaths in the series. Death followed infection in each instance. It is noted that these are mostly among earlier reports. An additional seven mothers (13 per cent) experienced stormy postpartum courses.
11. Postpartum bleeding occurred in eight cases. The excessive bleeding, seemingly, did not always arise from the cervix, but was secondary to uterine atony. It is remarkable that so few cases experienced excessive bleeding.
12. Sixteen stillborn infants are reported, a primary fetal mortality of 29 per cent.

Discussion

Rigidity of the cervix is mentioned in seventeen cases, and in all cases reported the failure of the cervix to dilate normally is the outstanding feature. The characteristic doughnut-appearing detached cervix becomes amputated when the cervix is approximately 3 to 5 cm. dilated.

Many writers have postulated a primary cervical rigidity, and the fact that 75 per cent of the cases reported were in primiparas and averaged 33 years of age would suggest this possibility. On the other hand, histologic examination of many cervixes show no primary structural differences from those of a normal cervix at term.

In 25 per cent of the cases reported, there was known cephalopelvic disproportion. This disproportion, with faulty mechanism of labor, we believe may cause secondary changes in the cervix which render it inelastic and unyielding. With impingement of the cervical tissue between the fetal head and the bony pelvis, congestion occurs with circulatory changes, leucocytic infiltration, and edema. Such changes were noted histologically in our specimen.

With the undilated, unyielding cervix pressed upon by the head, the active uterine segment pulls the inactive portion upward until finally a tear starts occurring at the cervicovaginal juncture, a line of cleavage develops, and continues until the separation is complete or practically so. A large portion retains a small attachment. A point of necrosis due to continued pressure on the cervix with ischemia is suggested, and this may occur. In our case there was no gross or microscopic evidence of such an area.

Five cases of amputation followed introduction of a rubber balloon. These cases perhaps should not be included in a report of spontaneous amputation of the cervix. Two were in cephalic and three in breech presentations. They, however, represent probable rigidity of the cervix in which the unyielding ring was pulled rather than pushed off from its original attachment.

Summary

Annular detachment of the vaginal portion of the cervix during labor is a rare complication.

The basic causes for the condition are an unyielding cervix, disproportion, and a faulty mechanism of labor. The unyielding cervix develops a circular line of cleavage and is torn away at its cervicovaginal junctura.

The fetal mortality has been extremely high (29 per cent). The high rate of stillbirths is due to the long labors, and the small pelvis, not cervical detachment per se.

In only one instance is spontaneous abortion mentioned as a sequel to cervical amputation.¹⁰ One would expect this to occur more often following amputation of the cervix. Our experience with pregnancy following cervical amputation is that spontaneous abortion occurs frequently.

Four women here reported had successful subsequent pregnancies and vaginal deliveries. Gilles²⁵ patient had five normal deliveries later. DeCosta's¹ patient was later delivered by elective cesarean section. The indication for section was the former long difficult labor and the amputated cervix. An elective cesarean section is probably the best way to manage subsequent pregnancies. There will be exceptions to this rule.

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SUBACUTE BACTERIAL ENDOCARDITIS DURING PREGNANCY

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ACUTE bacterial endocarditis developing during pregnancy is extremely rare. Stander notes in his book that a careful review of the literature reveals only 18 authentic cases. The introduction of penicillin has provided an effective means of therapy for this condition. The management of the pregnancy and this serious complication is of considerable interest to obstetricians and cardiologists. The careful reporting of individual experiences will provide some clinical data which may point the way to the most appropriate therapy.

The patient was first seen in her third pregnancy at about sixteen weeks. She was 31 years old and had two previous low or cervical cesarean sections for cephalopelvic disproportion in 1941 and 1943.

Her past medical history was essentially negative except for rickets. Her family history was irrelevant to her present complication. At the first prenatal examination all the physical findings, as well as the results of the laboratory procedures, were within normal limits. The only interesting finding was a high titer for brucellosis, 1:40.

The patient's prenatal course was uneventful until the pregnancy had progressed to about thirty-two weeks. She was spending the summer in upper Wisconsin and had a protracted sore throat which did not clear up on the usual medication. She was admitted to the hospital on Aug. 20, 1945, for study because of the following vague complaints: a feeling of lassitude, anorexia, night sweats, easy fatigability, epistaxis, roaring in the ears. The physical examination was negative except for the presence of a loud, harsh heart murmur replacing the first sound at the apex. This was not present at previous examinations.

The following studies were carried out at this time. Blood counts revealed a moderate anemia. In nose and throat cultures the usual flora was present with the exception of two colonies of *beta hemolytic Streptococcus*. The ear, nose, and throat consultants found an abnormal patency of the Eustachian tubes, probably associated with pregnancy, and an excoriation of the septal mucous membrane of the nose. The cardiologist thought that the heart murmur was associated with the anemia. An electrocardiogram revealed no pathology, but an x-ray of the chest for heart size showed it to be 40 per cent oversize. How much of this was the result of pregnancy could not be determined. It was thought that the high *Brucella* agglutinin titer, the opsonic index, and the phagocytic count were indicative of immunity rather than an active infection. Blood cultures for *Brucella* organisms and guinea pig inoculations proved negative subsequently.

The patient was discharged from the hospital unimproved for a few days during which she was asked to take her temperature every four hours. She continued to run a low grade temperature the level of which rose slowly so that she was readmitted on Sept. 4, 1945, for further study.

On September 11 the patient noticed that her finger tips had changed color, and she developed a transient numbness and tenderness. The heart murmur had become more pronounced. The size as measured by the x-ray had increased to 60 per cent above normal. Blood cultures were positive for the first

time and revealed a pure culture of *Streptococcus viridans* which was later identified as *Streptococcus salivarius* (Sherman classification). Repeat blood cultures on three successive days confirmed the diagnosis of subacute bacterial endocarditis.

She was started on penicillin therapy, receiving 125,000 units every three hours, or 1,000,000 units a day. Small blood transfusions were administered at frequent intervals. She became afebrile promptly and remained afebrile during her entire hospital stay, with the exception of the day following operation when the temperature rose to 37.6° C. The only noteworthy event occurred on September 17 when the patient complained of fleeting periods of amnesia, but these disappeared.

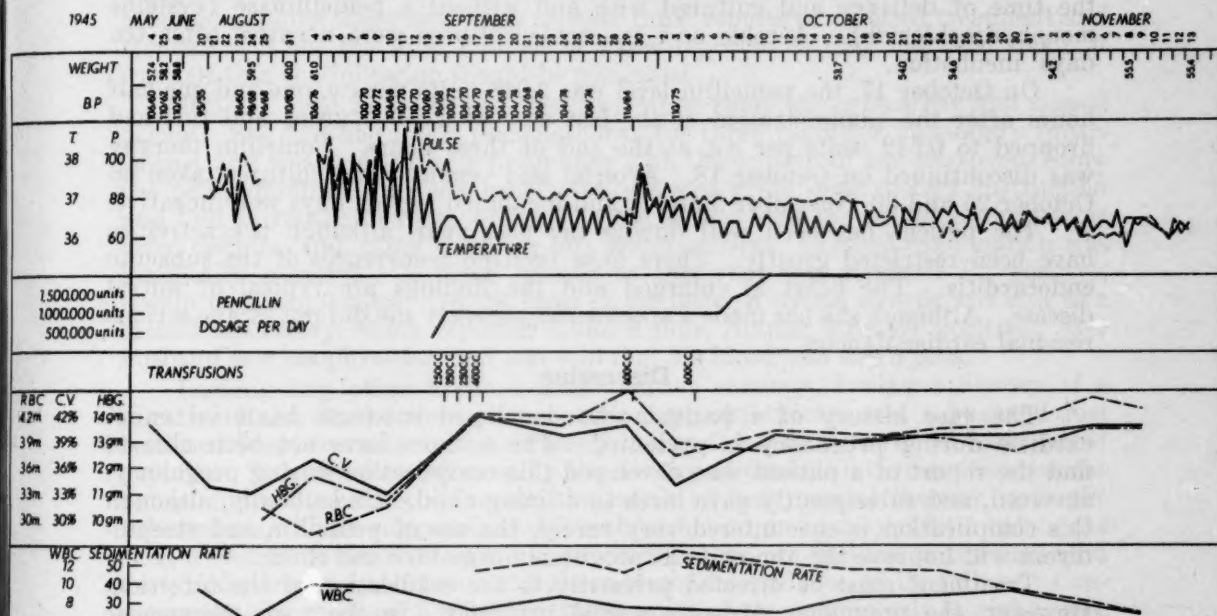


Fig. 1.

It was decided to terminate the pregnancy on Sept. 29, 1945. The baby was obviously viable, the active infection had subsided, and the heart would show no great improvement until the pregnancy was terminated. A cesarean hysterectomy was performed in order to decrease the hazard of postoperative infection and because this was her third abdominal delivery. She withstood the operation satisfactorily, and her recovery from this procedure was entirely uneventful.

A consultant who saw the patient suggested that the amount of penicillin be doubled, so that she received 250,000 units every three hours for the remainder of her treatment. Blood cultures, venous and arterial, sedimentation rates, blood counts were repeated at frequent intervals and can be followed in the graphic record.

Penicillin therapy was discontinued on October 18, the twentieth post-operative day and thirty-six days after it was started. She received a total dose of 45,850,000 units. The heart decreased in size slowly and the electrocardiogram showed a sinus arrhythmia and an occasional extrasystole. At the time of her discharge from the hospital on November 13, repeated arterial and venous blood cultures incubated for ten days were negative, the sedimentation rate was approaching normal, and the white count was normal.

Penicillin Studies

The organism, *Streptococcus salivarius* was found to be sensitive to 0.02 units of penicillin per cubic centimeter. The dose of 125,000 units of penicillin every three hours maintained an adequate level for two and one-half hours after its administration; the level was 1.025 units per cubic centimeter.

At the time of delivery the following penicillin levels were computed:

Maternal blood	2.048 units per c.c.
Cord blood	0.512 units per c.c.
Amniotic fluid	4.096 units per c.c.

Samples of maternal blood, cord blood and amniotic fluid were taken at the time of delivery and cultured with and without a penicillinase (cysteine monohydrochloride). Aerobic and anaerobic cultures were negative after ten days' incubation.

On October 17, the penicillin level was 2.048 units per c.c. one and one-half hours after the administration of the last dose of 225,000 units, and this had dropped to 0.512 units per c.c. at the end of three hours. Penicillin therapy was discontinued on October 18. Arterial and venous blood cultures taken on October 25 and 30, November 5 and 9, and incubated for ten days were negative.

The patient has been well during the past year, although her activities have been restricted greatly. There have been no recurrences of the subacute endocarditis. The heart is enlarged and the findings are typical of mitral disease. Although she has made a spectacular recovery she did not escape serious residual cardiac damage.

Discussion

The case history of a patient who developed subacute bacterial endocarditis during pregnancy is presented. The authors have not been able to find the report of a patient who developed this complication during pregnancy, survived, and subsequently gave birth to a living child. Undoubtedly, although this complication is encountered very rarely, the use of penicillin and streptomycin will improve the almost fatal prognosis for mother and child.

Treatment must be directed primarily to the eradication of the infection. However, the pregnancy presents special problems. In the past, therapeutic abortion was often advocated in order to improve the patient's ability to overcome the serious complication. Potent antibiotics which eradicate organisms from the bloodstream and keep it sterile, allowing the endocardium to recover from the infection, should make it possible to allow patients to continue their pregnancies to viability or longer. The eventual termination of the pregnancy can be carried out by the most appropriate method, but it must not be forgotten that the heart usually suffers irreparable damage. Delivery as well as subsequent childbearing must be considered in the light of the existing cardiac pathology.

Dr. Emmet Bay, Professor of Medicine, University of Chicago Medical School, was responsible for the medical management of this patient.

SYPHILIS IN PREGNANCY TREATED BY PENICILLIN*

C. H. INGRAM, JR., M.D., F.A.C.S., PITTSBURGH, PA.

(From the Department of Obstetrics, Western Pennsylvania Hospital)

SINCE the publication in 1943 by Mahoney¹ of the first use of penicillin in the treatment of syphilis, there have been many carefully controlled studies using this agent in practically all branches of syphilotherapy. In the field of prenatal syphilis there have been at least three reports of detailed treatment and results.²⁻⁴ Since the total number of cases reported to date has been small, it was felt that the following should be presented.

Mrs. G., aged 27 years, was first seen when three weeks past her first missed period. She had had a left pneumothorax for three years for pulmonary tuberculosis, and was attempting a pregnancy with the consent of her physician. Since the pelvic findings were not conclusive, she was given some dietary instruction and told to return in three weeks. At the second visit the pelvic findings were more definite, and, other than her left pneumothorax, physical examination was essentially negative. A blood sample at this visit was reported Rh positive, Group O, Kahn 3 plus. On the basis of the latter a second sample was sent to a second laboratory which reported Kahn 4 plus, Kolmer strongly positive. Her husband saw his physician and was told that his blood also was 3 plus.

Lacking any other findings than positive serology, having a history of a negative Kahn at the time of the original pneumothorax, and a husband just returned from overseas service, it was felt that this was a case of an early latent syphilis. This was strengthened by the history of penicillin therapy two months before for a dermatitis. Fearing the result of heavy metal therapy upon the tuberculosis, it was suggested that we abort her to avoid a syphilitic baby. As such a course would still leave an infected mother, we decided to try penicillin first, deferring the abortion until there might be evidence of its failure. Consequently, she received 2,400,000 Oxford units of the sodium salt in eight days. Ten days later the second laboratory reported the Kolmer still strongly positive, but the Kahn had dropped to a 3 plus. Another month later the Kolmer was clearing in the fifth tube and the Kahn had dropped to 2 plus. Fetal movements were first felt at about this time.

In a discussion of the case with a dermatologist, her physician was given a very gloomy prognosis, and a second course of treatment combining heavy doses of both penicillin and mapharsen was advised. In a desperate quandary, a summary of the case was sent to Dr. John H. Stokes. His prompt reply⁵ gave the opinion that the baby would be normal and that probably we had also cured the mother's syphilis. A note of caution was sounded in a subsequent communication in which attention was called to the fact⁶ that the newer penicillin is much less effective against the *treponema pallidum*, and suggested a second and heavier course of treatment in the event that quantitative Kahns failed to show steady improvement.

Following his suggestion, seven weeks from the end of treatment, a quantitative Kahn was 4 units, while the Kolmer did not go beyond the first tube. Meanwhile the pregnancy progressed uneventfully, and two months later a completely negative quantitative serology was reported.

A living female infant weighing well over 8 lb. was delivered by low forceps at term under nitrous oxide, oxygen, and a total of two ounces of ether. The

*Presented before the Pittsburgh Obstetrical and Gynecological Society, Dec. 9, 1946.

cord blood gave a 1 plus Kahn and a slightly positive Kolmer, but mother and baby progressed normally.

Six weeks post partum the maternal serology was negative, and one month later the baby's blood was also negative both Kahn and Kolmer. At the same time x-ray examination of three extremities showed normal bone architecture and no evidence of periosteal reaction.

A recheck of the mother's chest likewise showed no changes as a result of her pregnancy or anesthesia.

While continued observation has been advised, it now seems quite probable that both mother and baby are free of syphilis.

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6004 PENN AVE.

TUBAL AND UTERINE TWIN PREGNANCY*

MAURICE O. BELSON, M.D., F.A.C.S., BOSTON, MASS.

(From the Department of Gynecology, Tufts College Medical School and the Gynecological and Obstetrical Service of the Carney Hospital)

THIS case is being reported because it is unusual and rare. I have been unable to find any similar reports in the recent literature or in the standard textbooks.

Mrs. L. D., aged 35 years, gravida iv, para i, Rh positive. Menstrual periods occurred regularly every twenty-eight days, lasting three days, without dysmenorrhea. She had a right inguinal herniorrhaphy performed in April, 1937, and two years later in May, 1939, an appendectomy. On Jan. 31, 1941, she was delivered of a living male child by a Scanzoni maneuver after a twenty-hour labor with a persistent posterior head. Her convalescence was uneventful. During her second pregnancy she miscarried at two months, and a curettage was performed in September, 1943. The following year, in September, 1944, during her third pregnancy, she ruptured the membranes at twenty-six weeks and promptly started in labor and was delivered of male fraternal twins weighing two pounds, four ounces, and three pounds, two ounces, respectively. They survived approximately seventy-two hours.

In this present illness her last regular period had occurred on August 24, 1945. Six weeks later, on October 6, 1945, at 11:30 P.M., I performed an emergency operation at the Carney Hospital, removing an unruptured left tubal pregnancy. There were about 5 c.c. of free blood in the pelvis which had apparently leaked out through the fimbriated end of the tube. The right tube was normal, as were both ovaries. The pathologic report was: "Ectopic tubal pregnancy; chorionic villi showing regressive changes, trophoblastic giant cells with massive hemorrhage, and an acute inflammatory reaction in the wall of the tube. There is no evidence of malignancy."

At the time of the operation I observed that the uterus was slightly enlarged and made a note of it in the operative procedure. Her convalescence was uneventful except for the fact that she complained of more nausea than is usual postoperatively for an otherwise uneventful course. She was discharged home on the eleventh postoperative day.

Pelvic examination one month later at the office revealed a uterus enlarged to the size of a two months' gestation, although she had had no marital relationship since some time before the recent operation. She had not menstruated since her last regular period August 24, 1945. A Friedman test at this time was reported positive, confirming the diagnosis of intrauterine pregnancy.

She was placed on the usual prenatal regime with additional advice to have rest periods and to take special care to avoid overexertion of any type. Progesterone and vitamin E were also prescribed because of her past history.

In the latter part of January, 1946, when she was about four and one-half months pregnant, she was x-rayed for the possibility of twins because the uterus appeared to be larger than was consistent with her period of amenorrhea. X-ray confirmed the diagnosis of intrauterine twin pregnancy. About two weeks later she began to stain and then began to flow slightly. She was hospitalized im-

*Presented at the 18th Annual Meeting of the New England Obstetrical and Gynecological Society, Oct. 30, 1946, at Boston, Mass.

mediately. On questioning the patient she stated that for several days preceding this bleeding she had been entertaining friends from out of town and had been riding a good deal in automobiles and was obtaining very little rest or sleep. At the hospital she was placed on a regime of absolute rest in bed, large doses of progesterone, vitamin E, and sedation. The bleeding subsided and the patient appeared to be doing well, when on the ninth day in the hospital labor began and she was delivered of fraternal male twins at twenty-four weeks of pregnancy, on Feb. 20, 1946. The first infant weighed one pound, ten ounces, and the second baby weighed one pound, eleven ounces. The second twin lived only two hours, and the first twin survived for ten hours. The mother made an uneventful recovery.

**MARGINAL PLACENTA PREVIA TREATED BY ARTIFICIAL
RUPTURE OF THE MEMBRANES THIRTY-NINE DAYS
BEFORE VAGINAL DELIVERY**

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(From the North County Community Hospital)

IN THE following case a marginal placenta previa, diagnosed at twenty-eight weeks, was treated by rupture of the membranes, and the patient delivered vaginally thirty-nine days later. The 5 lb., 4 oz. baby lived.

The patient, a 35-year-old multipara, whose past history included a nephrectomy in 1940 for a tuberculous kidney, was delivered of her first infant as a normal primipara in January, 1945.

The present pregnancy, which was expected to be at term on July 17, 1946, was normal until she was approximately twenty-one weeks, at which time vaginal bleeding occurred at the end of a strenuous day. All bleeding ceased after bed rest for forty-eight hours. One week later she was allowed up progressively, only to have spotting occur after she had been out of bed seven days. The next three weeks, one in bed and two up, she was symptom free. Spotting then occurred. The patient was put back to bed. After she had been confined to her bed for two weeks profuse vaginal bleeding occurred, unaccompanied by pain on exertion. She was immediately hospitalized, as the length of her pregnancy and type of bleeding indicated a tentative diagnosis of placenta previa. As x-ray studies failed to locate definitely the placenta in the fundus, a pelvic examination was done. A vertex was presenting and dipping into the pelvis. The cervix was moderately thick, but admitted one finger. A marginal placenta previa was noted. Because of the unlikelihood of the baby surviving, the location of the placenta, the amount of bleeding which she had already had, and the type of cervix, it was deemed advisable to rupture the membranes. Two doses of infundin (one minim each), twenty minutes apart, produced some mild cramps and controlled the bleeding. Twenty-four hours later, when the patient had not gone into labor, but the bleeding was satisfactorily controlled, it was decided to attempt further induction by castor oil, rather than run the risk of a violent labor with more infundin. A cathartic effect was obtained, but no labor was forthcoming. The patient, therefore, was started on penicillin 20,000 units every three hours as a prophylactic measure. This was stopped after two afebrile weeks. During the thirty-nine days following the rupture of her membranes the patient continued to leak amniotic fluid, and on four occasions had a slight amount of bleeding, varying from a dram to half an ounce. Each time it was readily controlled with one dose of one minim of infundin. Frequent blood studies were made and four transfusions, as well as iron by mouth, were used to support her blood level. She had an easy two-hour and thirty-minute labor, being delivered under pudendal block anesthesia with low forceps, as the baby's head arrived on the perineum.

TRUE KNOT IN THE UMBILICAL CORD CAUSING DEATH OF MONOAMNIOTIC TWINS IN A PRIMIPARA BEFORE LABOR

JOHN B. BOYLE, JR., M.D. AND CHRISTIAN F. RICHTER, M.D., BALTIMORE, MD.
(From St. Joseph's Hospital)

MRS. E. R., a 20-year-old para 0, gravida i, was first seen by one of us (J. B. B.) on Mar. 16, 1942, stating that her last menstrual period had occurred on Nov. 20, 1941. Physical examination confirmed the diagnosis of pregnancy, and the date of confinement was estimated to be Aug. 27, 1942. No physical abnormalities could be found, and pelvic measurements were within normal limits.



Fig. 1.—Stillborn, macerated monoamniotic twins showing knotted cords causing death.

The prenatal course was uneventful until April 21, when slight spotting of blood appeared, and ceased with bed rest and sedation. Fetal movements were noticeable after four and one-half months. On June 30, there was an increase of blood pressure which fluctuated for the next two weeks between 134/94 and 140/100, with a trace of albumin present. With this increase of pressure heart sounds became inaudible. Examination every few days thereafter failed to reveal evidence of fetal life. On July 6, a flat plate of the abdomen showed twins in the vertex presentation.

The patient was admitted to the hospital on July 12 with irregular abdominal pains. There were signs of mild toxemia, her blood pressure was

135/95, with slight ankle edema, and a trace of albumin in the urine. The presenting part was unengaged, and fetal heart tones could not be located. X-ray of the abdomen at this time revealed overlapping of fetal skull bones. Treatment with bed rest, sedation, salt-free diet, and concentrated glucose resulted in recession of pressure, edema, and albuminuria. On July 14, a medical induction by castor oil, enema, and quinine was instituted. Gradually the pains became regular and labor progressed. At 7:00 A.M. on July 15, the membranes ruptured, and at 7:45 A.M. the first twin was delivered spontaneously in left occipito-anterior position, and five minutes later the second twin in right occipitoanterior presentation. Both were males, and were discolored and macerated, having apparently been dead for some time. The placenta separated spontaneously and delivered immediately. There was but one placenta with two cords, the middle thirds of which were intertwined and knotted, causing a cluster of knots the size of one's clenched fist.

The postpartum course was uneventful, and the mother was discharged on her seventh postpartum day.

Comment

We felt this case unusual and worth reporting inasmuch as it falls into that rare group of monoamniotic and uniovular twins, and in a primigravida prior to the onset of labor. The incidence of monoamniotic twins has been variously estimated by Müller at 1:6,000, and by Rosenberg at 1:60,000. In a review of the literature Quigley was able to find only 109 cases; torsion or true knot formation was reported 58 times, or in 53.2 per cent. Lundgren found 24 of 31 reported cases to be associated with multiparity. McNally has called attention to the misconception that fetal death occurs only during labor. Most writers on this topic are of the opinion that knotting occurs at the ninth to twelfth week of gestation, at which time the cord is sufficiently long and the fetuses small and active. The knots are tightened during labor, resulting in impairment or complete blockage of the fetal blood supply. Several authors comment on the formation of a knot in the cord of a second twin by delivery of the first.

There is little or no risk to the mother; however, Quigley mentions eclampsia four times in his 109 cases; both McNally's and our own case, in which the fetuses died prior to labor, were mildly toxic.

The separate cords of twins are especially adapted to intertwining and knotting if present in one amniotic sac. Atwood is of the opinion that knots formed during delivery are never serious—those formed early in gestation may prove fatal. In Quigley's series (109 cases), both twins survived in only 17 cases. Both twins died in 41 cases, and one died in 20 cases. Eight monstrosities died, the result in 23 was unreported, and 8 aborted, leaving 94 cases from which to estimate mortality. One hundred twenty-six fetuses of 94 twin pregnancies did not survive, leaving a 68 per cent mortality.

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Editorial

The Third American Congress of Obstetrics and Gynecology

The JOURNAL is pleased to announce the holding of a Third Congress devoted to the progress of this branch of medicine to be held in St. Louis, Mo., on Sept. 8 to 12 of the current year. In an editorial published in the February, 1937, issue, the attention of the profession was called to the need and desirability of holding such a Congress in a field to which American physicians and institutions had contributed so much and which should afford an opportunity for the inter-exchange of ideas, for the presentation of advances in methods and techniques, for the instruction of visitors, be they physicians, nurses, public health officials, for the display of scientific achievements and research products, for commercial exhibits. Two very successful and well-attended Congresses have been held, the first in Cleveland in 1939, the second in St. Louis in 1942. Both were sponsored by the American Committee of Maternal Welfare, as is the Third Congress now in process of formation. It promises to be equally successful. Committees have been organized to arrange the necessary details, and the programs thus far developed promise much of value to those who will attend the sessions. It affords unexcelled opportunities for instruction, for entertainment, for a gathering of minds.

Interest in the welfare of womankind is age-old and worldwide. No longer is such interest based merely on sentiment, on religion, on conventional standards; it depends today on knowledge and reason. That particular branch of medicine which is concerned with the productive life of women has grown and developed enormously in these last hundred years, but it has also involved and invaded many allied fields. These strides in medical and social progress may justifiably be recorded and disseminated through the medium of a National Congress to which the JOURNAL is prepared and desirous of giving its unqualified support.

Department of Reviews and Abstracts

Selected Abstracts

Malignancies

Gray, Layman A., Friedman, Milton, and Randall, William F.: Observations on Treatment of Adenocarcinoma of the Uterus, Surg., Gynec. & Obst. 82: 386, 1946.

Ten women suffering from adenocarcinoma of the uterus are presented without five-year follow-up. Six out of seven of the patients still had residual carcinoma at hysterectomy, in spite of the fact that they were treated with large doses of intrauterine radium; and three of these patients had metastases to the ovary, indicating the necessity for oophorectomy at the time of operation. The authors describe an instrument for application of intrauterine radium tubes which is designed to make the radium more effective. This instrument, termed by them a hystero-stat, makes possible the placing of the tubes both transversely and in lateral tandems. Of the ten patients treated, seven received extremely large doses of radium, namely, 6,030, 7,000, 7,000, 8,000, 8,900, 10,410, and 12,480 milligram hours. Hysterectomy followed the application of radium in thirty-eight days to six months. Six of these seven uteri showed residual carcinoma. The seventh showed no evidence of tumor and was the case treated with 12,480 milligram hours. Three of these patients had ovarian metastases. The authors conclude that radium alone is not sufficient to cure adenocarcinoma of the uterus. They are unable to state the exact role and specific indications for preoperative radium therapy.

L. M. HELLMAN.

Rojas, Daniel A.: Dysgerminoma of the Ovary, Bol. Soc. de obst. y ginec. de Buenos Aires 25: 33-56, 1946.

The author reports four cases of dysgerminoma of the ovary. Three of the patients were under 20 years of age, and one was 26 years old. In all of the patients menstruation was normal, and there were no abnormal symptoms. Three of the patients were virgins, and the fourth patient had previously had two children. In one of these labors she had dystocia because of the ovarian tumor.

Laboratory studies before operation revealed no special information. In three of the four cases a supravaginal hysterectomy was performed with removal of both adnexa. In one patient only the ovarian tumor was removed.

J. P. GREENHILL.

Nestarez, Oscar B., and Assali, Nicolau S.: Some Aspects of Cancer of the Endometrium; Its Association With Pregnancy, Obst. y ginec. latino-am. 4: 161-189, 1946.

Cancer of the body of the uterus is more frequent after the menopause. Pregnancy does not seem to have any effect on the development of cancer of the body of the uterus; neither do fibromyomas. On the other hand, glandular hyperplasia of the endometrium seems to have a connection with this type of cancer, particularly when it occurs during or after the menopause. The authors report a case of epidermoid cancer of the endometrium associated with pregnancy which was removed by means of curettage. They also report two cases of epidermoid metaplasia of the endometrium with beginning malignant degeneration in the first and polypoid hyperplasia with a malignant tendency in the second.

The authors mention that there are in the literature eight cases of cancer of the body of the uterus associated with pregnancy, including their own case.

J. P. GREENHILL.

Analgesia, Anesthesia

de Senarclens, Francois: **The Effect of "Dolantine" Upon Delivery**, *Gynaecologia* 121: 225-246, 1946.

Senarclens, of the St. Gall Obstetric Hospital, describes his experience with the intramuscular injections of 100 mg. of "Dolantine" (known as demerol in America), chemically the hydrochloride of 1-methyl 4 phenyl piperidine 4 carboxyl acid ethyl ester.

Dolantine is given at the onset of labor and repeated, if necessary, four hours later (seven cases). The author's series includes 167 cases, 127 primiparous and 40 multiparous. Sixty-one patients were less than 25 years of age; 85 cases, 26 to 35 years of age, and 21 had passed their 35th birthday.

The author states that pains were regular in type in 81 per cent of the cases, mediocre or poor in the remaining 19 per cent. The intensity of the contractions were classified as feeble in 8 per cent, average in 58 per cent, and strong in 3 per cent. The remaining 31 per cent were categorized as irregular. There was increased duration of labor pains in 10 per cent, no change in 44 per cent, and a decrease in duration in 33 per cent of the cases, while 3 per cent exhibited arrested contractions. The expulsive pains were considered good in 76 per cent, fairly good in 10 per cent, and poor in 14 per cent of the cases. The average duration of labor for the primipara group was fourteen hours, twenty-five minutes; while the multipara duration of labors averaged eight hours, fifty-five minutes.

Three per cent of the cases were subjected to cesarean section, 6 per cent to forceps delivery, and 4 per cent to trachelotomy among the obstetrical interventions. In 58 per cent of the cases the perineum required operative care—episiotomy in 30 per cent, repair of first degree tear in 10 per cent, and a second degree tear in 8 per cent.

Seventy-two per cent of the cases delivered their placentas normally; 23 per cent required fundal pressure—while six cases required manual removal. The blood loss was 500 Gm. or less in 78 per cent of the cases; 10 per cent lost 510 to 1,000 Gm.; 3 per cent lost 1,010 to 1,500 grams.

Febrile complications were present in 35 per cent of the cases (4 per cent febrile; 3 per cent endometritis; 7 per cent subinvolution; lochiometra, 2 per cent; mammary engorgement without abscess, 4 per cent; thrombosis, 2 per cent. There was one death of septicemia occurring eleven hours after delivery. Posterior pituitary extract solution was used intrapartum in 13 per cent of the cases, quinine in 7 per cent. Eighty-two per cent of the newborns were normal, and 2.25 per cent were "a little sleepy"; 6 per cent had asphyxia levida, and 2.25 per cent asphyxia pallida. Three per cent of the babies were born dead (2 macerated and 3 stillbirths) and an additional 2.25 per cent died in the neonatal period.

The author concludes—"the normal labor of the primipara and the multipara is relieved, accelerated, and rendered less painful" when "Dolantine" (demerol) is used. This drug was found most valuable in cases exhibiting pelvic disproportions where it exerted an effect similar to opiates but did "little harm to the mother and child."

C. E. FOLSOME.

Sauter, Hans: **The Effect of a Spasmolytic Used in the First Stage of Labor. Investigation of a New Drug, "Hexacompal,"** *Gynaecologia* 121: 247-268, 1946.

Sauter investigated a new spasmolytic preparation "Hexacompal" (a suppository containing paverine HCl 0.025, extract of belladonna 0.05, Allobarbitol 0.05, dimethyl amino antipyrine 0.30, and caffeine 0.30). He compared this preparation to spasmalgin (a combination containing paverine HCl 0.020, pantopan 0.01, and atrinal 0.001) and dolantine (known in America as demerol). The latter two are administered by intramuscular injection. The writer reports a much more improved uterine tone, with relief of spastic conditions and acceleration of the first stage of labor from the use of hexacompal as compared to the other two drugs.

The author found hexacompal suitable for tests of uterine contractility in early labor. He observed no untoward secondary manifestations from the drug's use. The contraindications and comparative considerations are detailed, including its use after thymophysin.

C. E. FOLSOME.

Collins, Selwyn B., Phillips, F. Ruth, Oliver, Dorothy F., with collaboration of Hingson, R. A., Vaux, Murray, and Lull, Clifford: *A Statistical Study of Delivery With Continuous Caudal Analgesia as Compared With Other Methods*, Pub. Health Rep. 61: Nov. 29, 1946.

This paper contains a detailed statistical analysis of the deliveries of 2,516 mothers under continuous caudal analgesia at the Philadelphia Lying-In Unit of the Pennsylvania Hospital during the period from May, 1943, through August, 1945. One thousand twenty-four deliveries by other than continuous caudal analgesia occurring during the period from December, 1942, through July, 1943, served as a control group. Although the control series is almost half the size of the caudal series, the distribution according to age and parity, complications, and type of delivery of the two series seems to be similar. It is to be noted, however, that the incidence of complications during delivery and the incidence of prolonged labors were slightly higher in the control than in the caudal group. Ninety and four-tenths per cent of the mothers in the caudal group received complete relief from pain, 4.3 per cent partial relief, and in only 5.3 per cent was there a failure of the method to relieve pain. The average duration of the caudal analgesia for primiparas was 3.7 hours, and 2.3 hours for multiparas. Drop in blood pressure of over 25 mm. occurred in 33.5 per cent of these mothers. There were two maternal group deaths in each group. Unfortunately, the details of these maternal deaths are not given. It is of interest to note that the incidence of mid-forceps is 8.4 per cent in the caudal group, while it is only 4 per cent in the control. Duration of the third stage was significantly shortened in the caudal group, and the incidence of febrile puerperium and subinvolution was also significantly reduced in the experimental cases. Of most marked interest, however, is the fetal outcome in these patients as compared with the control series. The percentage of infants who required a special agent to induce respiration was significantly reduced in the caudal group and, although the per cent net gain in weight by the seventh day was not significantly greater in the caudal cases, it did show some increase which indicated a trend. In the caudal group the stillbirths amounted to 9.1 per thousand live births as compared with 24.8 per thousand for the control. Similarly, the neonatal deaths were 11.5 per thousand live births in the caudal group as compared with 20.8 per thousand in the control. Thus, the total stillbirths and neonatal deaths were 20.6 per thousand in the experimental group as compared with 45.6 in the control. This is definitely a significant difference. The difference in stillbirths and neonatal mortality rates between the caudal and control group is still significantly different when the infants are divided into full-term and premature infants.

L. M. HELLMAN.

Endocrinology

Dodds, E. C.: *Estrogens in Cancer*, Schweiz. med. Wehnschr. 842: number 37/38, 1946.

The author briefly reviews the development of potent substances with estrogenic properties, both natural and synthetic. The latter includes stilbestrol, hexsterol, and dienestrol.

Huggins was the first to administer stilbestrol to patients suffering from cancer of the prostate. Other workers have confirmed the fact that about 95 per cent of these patients will respond in some degree to treatment, experiencing relief of pain due to pressure on nerves and frequently to urinary obstruction; likewise the level of acid phosphatase is reduced. There usually results an improvement in the patient's general condition, and in some cases a reduction in the size of the primary tumor and the secondary deposits. One does not claim synthetic estrogens to be a cure for cancer of the prostate; however, more

than palliation occurs, for there is a definite arrest, if not regression of the disease. Side effects are rarely sufficient to require that the treatment be abandoned. A daily dose of 1 to 5 mg. has been used. The mode of action is unknown. The changes in serum level of acid phosphatase would indicate an interference with the metabolism of the malignant cells. Huggins felt that if the activity of estrogens in the malignant cells of the prostate could be inhibited, then the growth of primary and secondary tumors would regress.

L. M. RANDALL.

White, Abraham: Preparation and Chemistry of Anterior Pituitary Hormones, Physiol. Rev. 26: 574-608, 1946.

White of Yale re-evaluates the anterior pituitary hormones. Upon the basis of physiologic evidence he states that there appear to be at least six recognized individual hormones, although there exists some biological overlapping among certain of the anterior pituitary secretions. Four of these protein hormones have been isolated in a homogeneous and highly purified state through the application of protein chemical techniques. These four include the lactogenic, the adrenotrophic, the growth, and the luteinizing hormones. The thyrotrophic principle has been isolated in highly purified form, but has not been examined by rigid criteria of protein purity. The follicle-stimulating hormone awaits further purification.

The author is of the opinion that success in the isolation and characterization of these anterior pituitary hormones has been related to advances in knowledge of protein chemistry. He states the biological activity seems to be intimately related to the protein nature of the active principle, and procedures which alter the protein structure even slightly result in a partial or complete loss of physiologic characteristics. A notable exception is the adrenotrophic hormone.

Efforts to detect in the protein hormones nonamino acid groups or active groupings of amino acids to which hormonal function could be assigned have been unsuccessful. At least three of the active principles, i.e., the thyrotrophic, the follicle-stimulating principle, and the luteinizing hormones contain carbohydrate in their structure. The inhibition of hexokinase by crude anterior pituitary extracts suggests the possibility of an important test system, by the use of both purified proteins and of models of known structure. This approach would be possible to the problem of the relation of protein structure to hormonal action.

White concludes that certain physical and chemical differences exist among anterior pituitary hormones isolated from different species. These variations are most striking by a comparison of the data for the luteinizing hormone preparations obtained from hog and sheep pituitaries; beef and sheep thyrotrophic hormonal proteins seem to be different. There exist also slight variations in the lactogenic hormones from beef and sheep glands. On the other hand, the purified hog and sheep adrenotrophins, although isolated by different techniques, appear to be identical in every property examined.

C. E. FOLSOME.

Munro, S. S., and Kosin, Igor L.: Relative Potency of Certain Synthetic Estrogens When Administered Orally to Chicks, Am. J. Physiol. 147: 582-590, 1946.

The authors evaluated the relative estrogenic potency of six synthetic estrogens biologically in young white Leghorn chicks. The estrogenicity of these compounds apparently increased with increasing saturation in the aliphatic block of the molecule (i.e., "open chain" portion of the molecule) and with methylation of the side chains (addition of methyl groups, CH₃).

The descending order of potency of the six compounds within the dose range used, three levels of 10, 20, and 30 mg. per pound of mash feed, was as follows: dianisylhexane (dimethyl ether of hexestrol), dianisylhexene (dimethyl ether of diethylstilbestrol), hexestrol, dienestrol, dienisylhexadiene (dimethyl ether of dienestrol), diethylstilbestrol.

The writers found that the degree of variability in oviduct response rose with the increased dose level of estrogens. They observed also that the growth rate of chickens greatly

affected the degree of oviduct response. They stressed need for adequate numbers of test animals and the necessity of several dosage levels when using this bioassay method to compare the potency of estrogens.

C. E. FOLSOME.

Tschumi, Rene: The Influence of Vitamins and Endocrines Upon the Physiology of Sperm Motility, Gynaecologia 121: 169-203, 1946.

Tschumi, working in Joels laboratory and the Women's Clinic at Basel University, contributes observations upon the direct influence of certain compounds upon human sperm motility. Among the substances used were certain vitamins: thiamine, riboflavin, pyridoxine, nicotinamide, ascorbic acid, and sodium tocopherol phosphoric acid esters; certain endocrine agents, thyroxin and posterior pituitary solutions; and, also the chemical intermediary acetylcholine.

The author adds pertinent data on sperm suspension substrates through his comparative evaluation of isotonic Ringer's solution and Baker's solution besides observing, in addition, the influence of dilutions of each of the above compounds in concentrations of 0.001; 0.01; 0.1 and 1.0 per cents using Baker's solution as the control in each experiment. In the forepart of his paper, Tschumi outlines his detailed methods using sperm from 12 males, aged 24 to 39 years. He reports that motility is prolonged upon the dilution of isotonic saline and glucose solutions, and the quality of motion is improved.

Baker's solution was found more useful as a sperm suspension than Ringer's solution; the former produced unusual improvement in motility, increased the number of motile sperm, and, in some instances, prolonged the motility as long as 700 hours, while Ringer's solution served primarily as a preservative substrate. Daylight exerted a shortened ability of sperm migration in a specially devised capillary tube as compared to sperm migrating upon the tubes in darkness—an important observation for future workers to remember. The elevation of the substrate to body temperatures decreased the sperm migration in capillary tubes but increased the intensity of motility.

Thyroxin, nicotinamide, and vitamin E, and, to a less extent, thiamine, all seemed to exert a tendency to favorably increase the distance travelled by sperm while ascorbic acid, acetylcholine, and posterior pituitary solutions seemed to exert no effects. The riboflavine and pyridoxine demonstrated an inhibitory effect upon motility. The article is well documented with 20 graphs and four tables.

C. E. FOLSOME.

Goldzieher, Max A.: The Effects of Estrogens on the Senile Skin, J. Gerontology 1: 196, 1946.

According to observations made previously by other investigators, topical application of estrogen has been known to prevent genital atrophy and to restore the normal state of the mucous membranes of the external genitals. In view of these experiments, the author has determined the effect of estrogen in an ointment base on restoring normalcy to the senile skin. The experiments were carried out on five elderly patients using estradiol and diethylstilbestrol and compared with three additional patients as controls. In two cases, the potency of the ointment used assayed at 10,000 I.U. of estradiol per ounce. In the other three patients, one miligram per ounce of diethylstilbestrol was administered. The hormone-containing ointment was rubbed in by gentle stroking daily for five minutes over a period of six weeks. Biopsies of skin were studied in the five cases to compare the structure of the aged skin before and after topical application. The treated skin showed pronounced regeneration of the surface epithelium. The number of cell layers was increased, and the wavy configuration of the epidermis was restored. The water content of the estrogen-treated skin appeared greater, and the elastic fibrils were more numerous. Biopsies from the skin of the control group showed no appreciable changes. The author feels that topical application affects the skin to a much greater degree than oral or parenteral application because the estrogen is not lost through body excretion, is not deactivated by the liver, and is not used

preferentially by the genital tissues. It appears likely that estrogens may be used for the correction of pathologic changes in the skin other than those directly caused by estrogen deficiency.

EDWARD C. HUGHES.

Endometriosis

Kahampää, V.: Upon the Pathogenesis of Ovarian Endometriosis, Acta obst. et gynec. Scandinav. 26: 139-160, 1946.

Kahampää describes in considerable detail the histopathologic findings of operative specimens taken from six cases of ovarian endometriosis and hemorrhagic cysts on the Second Women's Clinic at Helsinki.

The author agrees fully with Sampson's observations and opinion as to pathogenesis. However, he stresses the importance of follicular rupture and extravasation of blood in tissues in the development of a superior substrate for the subsequent implantation and survival of endometrial tissue fragments. His studies agree unusually well with similar findings, on the latter aspect, of Philipp and Huber.

The writer concludes that his 15 photomicrographs and studies showing evidence of better substrate to the subsequent growth of misplaced endometrial cells eventuating in ovarian endometriosis constitute valuable and substantial proof toward further confirmation of Sampson's implantation theory.

C. E. FOLSOME.

Fallon, John: Endometriosis in Youth, J. A. M. A. 131: 1405, 1946.

The author reports nine cases of endometriosis in teen age girls among the last 225 patients with proved endometriosis who were seen in the Fallon clinic (4 per cent). The youngest was 13 years of age.

The cardinal symptom was increasing dysmenorrhea.

The diagnosis of endometriosis should enter into the differential diagnosis of abdominal pain as soon as menstruation has been established. The author emphasizes the fact that endometriosis is a sterilizing disease, and tends to occur after about five years of incomplete sexual function, that is, menstruation without pregnancy, and these years are most likely to be the first five after the onset of menstruation.

The authors advise that menstruating females who are being operated upon for appendectomy should be operated through a median incision to allow light enough for inspection of the deep pelvis.

WM. BERMAN.

Yin, Y. C.: Endometriosis and Adenomyosis, West. J. Surg. 54: 490, 1947.

Endometriosis and adenomyosis are thought to be of different origins. They differ slightly also in histopathology and symptomatology. Both conditions are activated by high estrogen levels in the blood. It is suggested, and a case report demonstrates the validity of this suggestion, that the complete removal of one ovary and resection of most of the opposite ovary may result in involution of the implants.

The author feels that implantation occurs as the result of reflux menstruation, and that in such cases implantation is favored by high estrogen levels. In adenomyosis it is felt that the aberrant tissue is congenital in origin.

WILLIAM BICKERS.

Gynecology

Sauramo, Hannes: On Ovarian Hemorrhages With Special Reference to Intra-Abdominal Hemorrhages From the Corpus Luteum, Acta obst. et gynec. Scandinav. 26: 105-118, 1946.

Sauramo, of the Second Women's Clinic, University of Helsinki, reviews Bauman's 300 cases of ovarian hemorrhage, collects 292 additional cases from the literature and adds 2 cases of his own. In the one case the patient experienced a severe intraabdominal hemorrhage from

a ruptured corpus luteum cyst on the 21st day of a cycle. The second case was also accompanied by severe shock from rupture of corpus luteum cyst, crow-egg size, occurring on about thirtieth day of the cycle. In the collected 292 cases the author reports a mortality of 0.7 per cent.

C. E. FOLSOME.

Kleitman, R.: On the Question of Disgerminoma Ovarii, Robert Meyer Type, Acta obst. et gynec. Scandinav. 26: 85-104, 1946.

The author reviews three cases of disgerminoma ovarii, R. Meyer, observed during the past thirteen years at the Gynecology Clinic of the Public Maternity Hospital, Stockholm.

One case, incompletely operated upon, and treated with radiation therapy, died two years later. A second case submitted to bilateral salpingo-oophorectomy, had no radiation treatment, and is in good health six years after the surgery. The third case, from whom was removed a right ovarian tumor of this type, subsequently has had three pregnancies and good health during the past five years.

The author stresses the value of Föderl prognostic indications based upon the degree and type of necrobiotic changes of the tumor cells found in lymphatics to the individualization of therapy.

C. E. FOLSOME.

Kleitsman, R.: A Contribution on the Pathology and Clinical Aspects of Granulosa-Cell Tumors, Acta obst. et gynec. Scandinav. 26: 60-84, 1946.

Kleitsman describes in detail, using six photomicrographs, five cases of granulosa-cell tumor, observed during the past thirteen years at the Gynecology Clinic of the Public Maternity Hospital, Stockholm. Four cases were benign and occurred unilaterally and, according to Kleitsman, do not result in metastases or recurrences. The author feels an important clinical symptom of the benign granulosa-cell tumors is the endometrial hyperplasia which in women *before* the menopause is linked with amenorrhea and possibly metrorrhagia, but in postmenopausal cases with irregular hemorrhages. In the benign tumors the author concludes postoperative roentgen treatment is unnecessary.

C. E. FOLSOME.

Sorba, M.: Gonadotropins and Ovarian Tumors. Gonadotropinuria in a Case of Primary Polyembryonic Dysembryoma and Chorionepithelioma with Incomplete Precocious Puberty, Gynaecologia 122: 53-67, 1946.

Sorba reviews the extant literature of ovarian tumors exhibiting urinary gonadotrophic activity. He adds a case of a two-year-old female infant. The child, during a six-month interval, complained of intermittent abdominal discomfort, gradually developed a large abdominal mass. She was subjected to usual methods for diagnosis. It remained for exploratory laparotomy to reveal a primary right ovarian tumor (1,420 Gm.) with obvious metastasis to the right iliac and aortic lymph node chains. A similar type tumor, walnut sized, was found on the left ovary.

The first microscopic diagnosis, by J. F. Nicod, was malignant dysembryoma. Subsequent study classified the tumor as an embryonal teratoblastoma with chorionepithelioma.

The uterus and the breasts were enlarged, indicating functional activity of the tumor. The urinary gonadotropin curve was similar to that encountered in certain testicular tumor exhibiting metastases. The postoperative fall was followed by a subsequent rise, indicating further metastatic development, which later value dropped to normal values (less than 2 units per liter) just before death. Autopsy was not granted.

C. E. FOLSOME.

Correspondence

Anteversion of the Retroverted Uterus

To the Editor:

In his article on the procedure for anteversion of a retroverted uterus in the November issue of the JOURNAL, Dr. Carl T. Javert states, "The importance of correction of malpositions of the uterus is beyond the scope of this article, yet the improved chances of conception, prevention of spontaneous abortion, relief of nausea in pregnancy, alleviation of backache, and treatment of the incarcerated pregnant uterus are acceptable indications."

Is it true that the above are acceptable indications for the replacement of a retroverted uterus?

1. What proof is there that in a woman who has never been pregnant anteverting the uterus will help her to become pregnant? Although I have known a woman who has had a child become pregnant after anteverting her uterus, I have never known sterility to be cured by this device in a woman who has never been pregnant.

2. Is there any real proof that spontaneous abortion is the result of retroversion? This idea was once held, and passed on from textbook to textbook, but my own impression is that, allowing for the ratio of retroversion to anteversion in the female public, spontaneous abortion is no more common with retroversion than with anteversion.

3. It used also to be taught in the textbooks that nausea of pregnancy could be caused "reflexly" by a retroverted uterus. Is this idea still held by anyone with experience? If so, what is the proof?

4. Does anteverting a retroverted uterus cure backache? Very occasionally backache that is strictly localized over the "gynecologic" area may be cured by this procedure—but how often is even "gynecologic" backache cured by it?

5. In approximately 4,000 obstetric cases I have seen only an incarcerated retroverted uterus once. Is it therefore good obstetrics to antever all the retroverted pregnant uteri that present themselves because one in 4,000 will become incarcerated.

I have for some time been warning my students against the temptation that will beset them after graduation to join with their brethren in doing their share of the really atrocious number of useless suspensions at present being done. But when they can go to the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY in their library and see the printed word that I have quoted from Dr. Javert above, of what avail my warning?

H. B. ATLEE, M.D.

118 SOUTH PARK STREET,
HALIFAX, N. S.
DEC. 9, 1946.

Reply by Dr. Javert

To the Editor:

The focal point of the article in question is clearly stated in its title, and is elaborated in the text. An illustration was presented for further emphasis. Dr. Atlee ignores the theme of the article which deals with a method and concentrates on one sentence regarding "acceptable indications" for use of the method. Realizing the controversial nature of these indications and wishing to avoid a discussion of them, the writer stated that their importance was "beyond the scope of this article."

Evidently these indications are not acceptable to Dr. Atlee, judging from his letter, as well as his statements in the literature. However, the author mentioned them because they are the accepted opinions of American authorities on the subject, and the ones which he has been taught. Inasmuch as Dr. Atlee disagrees with these accepted indications for the use of a pessary, the burden of proof is upon him. The writer agrees with Dr. Atlee that the indications may be open to question, and for that very reason, when an opportunity arose to test them, he did so in a small series of patients, under the following circumstances.

During World War II, civilian dependent care placed an added responsibility on medical officers. Facilities for hospitalization of patients with abortion, nausea, and vomiting, backache with retroversion (even those relieved by pessary), and for the study of sterility, were not available. Often one was hard put to care for these conditions in the outpatient clinic. Under such circumstances, one wished to leave no stone unturned in doing the utmost to relieve the patient's symptoms or complaints. Moreover, there was an important morale factor (the soldier husband) to be considered. The number of patients seemed too small (there were fifty-five) for a statistical breakdown into the various categories, so it was not done. The Post Surgeon concurred in making the report as a worth-while experience, and it was sent through the customary military channels for approval, which was granted.

Subsequent experience with the combined procedure has shown its value. The author has been impressed with the ease with which a pregnant uterus turns over in the knee chest position, whereas the nonpregnant organ has resisted attempts at complete correction on several occasions, and only a semireposition has been obtained.

The pessary is not used frequently enough in patients with uterine retroversion, perhaps because not every doctor knows how to replace a uterus and insert a properly fitting pessary. That may be the reason for their failure to get the expected results. Realizing this, the writer dared to hope that the use of the combined procedure (which he has seen others employ with variation for over a decade) would facilitate replacement of the uterus. By no means does the writer recommend the pessary for every case of retroversion. He stated that lack of symptoms was a contraindication to its use in nonpregnant women. Asymptomatic retroversion is perhaps as common as symptomatic displacement.

Dr. Atlee's letter also makes reference to the article in connection with the "atrocious number of useless suspensions being done at present" and fears that the printed word as quoted from the writer's article will mislead his students. The writer agrees with Dr. Atlee that perhaps many suspensions are done needlessly. However, the article in question makes no mention of the "accepted indications" in terms of the suspension operation. The writer does wish to state that if these indications exist, and the pessary has provided a satisfactory therapeutic test, that a suspension operation should be given consideration in the treatment of selected patients.

There is certainly no harm in permitting students to learn of the medical opinions of others, even if they are contrary to the opinions of local authority. The writer encourages students to obtain opposite points of view. Didactic teaching has no place in clinical obstetrics and gynecology. All too often does time prove such teaching to be in error. The opposition of members of the profession to the contagiousness of childbed fever and anesthesia are examples. The writer believes in the saying attributed to Voltaire, that he may disagree with what has been said but will defend unto death the right to say it.

I will try to discuss these "acceptable indications" in greater detail.

1. *Sterility*.—Dr. William H. Cary, an outstanding American authority, states in a personal communication that he corrects a retroversion if it is present and inserts a pessary. Collectively, we have seen pregnancy follow such a simple procedure in approximately twelve patients, one of which occurred in the past month. Cary is of the opinion that the cervix is best exposed to the seminal pool if the uterus is erect, thereby facilitating spermigration. Dr. Atlee reports (*Canad. M. A. J.* 53: 122, 1945) a suspension operation on a sterility patient. He does not state whether a preliminary trial had been given the pessary.

2. *Spontaneous Abortion*.—Dr. H. J. Stander states in his textbook (ed. 9, p. 650), "Abortion is common in pregnancies complicated by retrodisplacements." It may not be

the retroversion per se, but the concomitant edema of the endometrium that is responsible. The same author states on page 736: "Displacements of the uterus, more particularly retroflexion and prolapse, are justly considered as important factors in the causation of abortion." Stander continues on page 742: "Prophylactic treatment is most important although, as a rule, it is not available in women aborting for the first time. After the patient has recovered from an abortion, a careful local and general physical examination should be made and, in case any abnormality is discovered, the necessary curative or precautionary measures should be instituted before renewed conception occurs. If the uterus is retroflexed, the organ should be replaced and held in position by a properly fitting pessary." Curtis states in this connection (ed. 5, p. 451): "A uterus which is temporarily retrodisplaced, and enlarged and congested, such as is encountered after abortion and in the puerperium, may be satisfactorily treated with simple measures. The pessary, despite its waning popularity, finds itself of greatest usefulness in these cases."

In addition to using the pessary in certain patients with retroversion who have had repeated spontaneous abortions, other therapy is employed including hormones, vitamins, and dietary measures.

Dr. Atlee states (Canad. M. A. J. 37: 547, 1937), "A retroverted uterus can be disregarded in the postpartum examination."

3. *Nausea and Vomiting of Pregnancy.*—In Stander's Clinic, such patients are treated with intravenous glucose, sodium lactate (if necessary) and small feedings. The uterus, if retroverted, is replaced as an adjuvant to this therapy. Using such a regimen, therapeutic abortion has been unnecessary for vomiting of pregnancy since 1938 (Kuder and Finn, AM. J. OBST. & GYNEC. 49: 762, 1945). Stander states in this connection (ed. 9, p. 578), "When abnormalities of the generative tract are discovered, they should be corrected, the displaced uterus should be replaced and held in position by a properly fitting pessary."

Dr. Atlee has stated (Canad. M. A. J. 41: 750, 1934) that pernicious vomiting is always a neurotic manifestation. He reported 33 cases treated by suggestion, three of whom required therapeutic abortion.

4. *Backache.*—Curtis says (ed. 5, p. 451), "A patient with bad retroversion may suffer from backache and bearing down discomfort." The same author states on page 602, "Backache is quite often caused by retrodisplacement and is relieved by its correction."

Dr. Atlee states (Canad. M. A. J. 53: 122, 1945) that a suspension failed to relieve a patient of backache, pain, and weight in the pelvis. It is quite possible that manual replacement and a therapeutic trial with a well-fitting pessary would have given the same information.

5. *Incarcerated Uterus.*—Dr. Atlee states that he has seen an incarcerated uterus only once in 4,000 cases. At the New York Lying-In Hospital, where nearly that many patients are delivered yearly, one is in a position to see uterine incarceration more frequently. The writer has observed this complication at least 12 to 15 times on the ward service, in his own cases, or those of other attending obstetricians. Dr. Erwin Smith and the writer replaced an incarcerated uterus successfully in the past month, without anesthesia, thereby relieving the patient's symptoms.

CARL T. JAVERT, M.D.

530 EAST 70TH STREET,
NEW YORK CITY.
JANUARY 20, 1947.

A Suggestion for Relief of Pain in Episiotomy Wounds

To the Editor:

A certain number of women complain of pain in the episiotomy wound as being the most uncomfortable thing in their postpartum course. The use of fine catgut, the loose tying of sutures, and the avoidance of too much catgut will do much to make the postoperative course less painful. Silkworm gut seems to cause more discomfort than other suture material. In spite of all these measures, there still exists discomfort in a considerable number.

A solution of equal parts of Tr. Merthiolate and 2 per cent Nupercaine solution sprayed on the episiotomy wound was found to be effective in alleviating discomfort for two to three hours. It may be repeated as necessary.

In these days of shortage of nurses, etc., there are times when optimum perineal care may not be given. The use of this spray would thus serve a twofold purpose.

MILTON M. ROZAN, M.D.

LANSING, MICHIGAN
FEBRUARY 7, 1947

Items

American Board of Obstetrics and Gynecology, Inc.

Examinations

The next oral examination and annual meeting of the American Board of Obstetrics and Gynecology, Inc., will be held at the Hotel William Penn, Pittsburgh, Pa., June 1 to 7, inclusive.

The following associate examiners have been appointed to assist the Directors of the Board: Dr. W. C. Danforth, 636 Church St., Evanston, Ill.; Dr. John L. Parks, Gallinger Municipal Hospital, Washington, D. C.; Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland, Ohio; Dr. S. A. Cosgrove, 88 Clifton Place, Jersey City, N. J.; Dr. L. M. Randall, Mayo Clinic, Rochester, Minn.; Dr. Nicholson J. Eastman, Johns Hopkins Hospital, Baltimore, Md.; Dr. Conrad G. Collins, Tulane University, 1430 Tulane Ave., New Orleans, La.; Dr. William J. Dieckmann, 5841 Maryland Ave., Chicago, Ill.; Dr. C. B. Lull, 807 Spruce St., Philadelphia, Pa.; Dr. J. R. Eisaman, 121 University Place, Pittsburgh, Pa.; Dr. Herbert E. Schmitz, 25 E. Washington St., Chicago, Ill.; Dr. Edward A. Schumann, M.D., Philadelphia, Pa.; Dr. Ward F. Seeley, M.D., Detroit, Mich.

The following physicians are to be included in the list of diplomates certified by the American Board of Obstetrics and Gynecology: Dr. Earle Milliard Marsh, 17 William Street, Rockville, Md.; Dr. Kenneth Anthony O'Connor, 109 Euclid Place, Oak Ridge, Tenn.

Third American Congress of Obstetrics and Gynecology

The program of the Third American Congress on Obstetrics and Gynecology to be held September 8 to 12, 1947, in St. Louis will feature general sessions for all groups making up the Congress, as well as smaller individual group meetings and round table discussions. The morning sessions will be panel-type presentations of the following subjects: Tuesday, Sept. 9: Anesthesia and Analgesia; Wednesday, Sept. 10: Cancer; and Thursday, Sept. 11: Cesarean Section.

The afternoon meetings of the medical section of the Congress will consider on Tuesday: Psychosomatic Aspects of Pregnancy; on Wednesday: Pregnancy Complicating Cardiac Disease, Diabetes and Tuberculosis; and on Thursday: Recent Advances in Endocrinology.

Round table discussions from 4 P.M. to 5 P.M. daily will consider such topics as etiology of abortion, asphyxia, fibroids, prolonged labor, infertility, early ambulation, adolescence, treatment of abortion, genital relaxation, ovulation, the menopause, the cystic ovary, uterine bleeding, nutrition in pregnancy, geriatric gynecology, endometriosis, and erythroblastosis.

Concurrent sessions and round tables for nurses, hospital administrators, and public health workers are being arranged.

The popular forceps and breech demonstrations that attracted so much attention at the Second Congress in 1942 will be increased in number so that eighteen demonstrations per day will be held, six each at 9:00, 1:00, and 5:00 o'clock daily.

A large Scientific and Educational Exhibit is being set up under the direction of Dr. J. P. Pratt of Detroit and a comprehensive Motion Picture Program is being arranged by Dr. John Parks of Washington, D. C. The committees assisting these doctors will review applications by prospective participants late this spring. Anyone wishing to make application for space in the Scientific Exhibit or for time on the Motion Picture Program may obtain the proper blanks from the office of the Congress at 24 West Ohio Street, Chicago 10, Illinois.

International Congress of Obstetrics and Gynecology Dublin, Ireland, July 7 to 12, 1947

The program for the Congress includes seven sessions to be devoted on successive days to the following topics: history of midwifery, puerperal sepsis, eclampsia, sterility, fetal and neonatal mortality, and shock in obstetrics. Representative speakers from several countries will discuss these topics, including the British Isles, New Zealand, the United States, Australia, South Africa, Sweden, Palestine, Denmark, Canada, and elsewhere.

Information about travel routes, hotel accommodations, etc., may be obtained from the local offices of Messrs. Thos. Cook and Sons.